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AGING PROCESS IN EYE AND ADNEXA

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Today the life expectancy at birth of a white child born in the United States is between sixty and sixty-five years. Negroes average about ten years less.[1] Fifty years ago the average expectation of life for white persons was forty-five years.[1] This change has come about through the control of communicable diseases, improvements in public sanitation, establishment of better nutrition and other advances that affect health.[1]

Between 1930 and 1940 the number of persons in the United States over 65 years of age increased by nearly 2,500,000 in a total population of 130,000,000. These figures indicate that ophthalmologists will be concerned increasingly with the treatment of the eyes of the aged.

Although the life of man may be divided into the stages of evolution, maturity and involution, the aging process is really continuous from birth to death and shows great individual variation. Carrel[2] said:

> We must know the physiological age of the patient, because his chronological age is misleading. It appears that the only possible method for measuring old age must be based on certain physiological and chemical modifications which occur in blood serum. [Therefore, we must look to the biochemist for knowledge of the aging process, which is usually accepted as inevitable.—C. B.] During the course of life, blood serum undergoes a progressive change, and becomes more and more inhibiting to the growth of colonies of tissue cells. This is a significant phenomenon and can easily be measured. The process of aging is very rapid at the beginning of life, as Minot showed long ago, but towards the end of life it takes place very slowly.

The cycle of change conditioned by the "vital force" which unfolds from birth to death varies in animals of different species and in individuals of

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1. Schools and the 1940 Census, Research Bulletin 19, National Education Association, 1941, p. 207.

2. Carrel, A.: The Mechanism of Senescence, Bull. New York Acad. Med. **45**:1144, 1928.

the same species. The horse and the dog, among the animals, have a vital force of shorter duration than man and the elephant. Family tendencies to longevity are well known.

With the possible exception of the tortoise, man probably has a longer life expectancy than any animal known,[3] and changes which are the result of senility are likely to develop. However, because a person is chronologically old is insufficient reason to diagnose the condition as a senile lesion. All toxic factors must first be eliminated. I have long believed, as does Crisp,[4] that the extent to which changes commonly regarded as senile are really due to infection or other extraneous influences may often be in doubt. There are many persons who age prematurely and some whose aging processes are retarded. The same is true of mental senescence, and Stieglitz[5] has pointed out that, although mental senescence may be premature in some persons, in others the continued brilliance of the intellect appears to defy the corporeal senility. He quoted Osler as saying that, "A man is as old as his arteries," but he stated the belief that it would be equally sound to say that he is as old as his vision or as his imagination. Many senile persons do not experience aging of the blood vessels and never exhibit an arcus senilis. For this reason many so-called senile changes probably should be grouped among diseases and not among simple senile degenerative changes. The fact that heredity plays a part in many anatomic congenital malformations, such as microphthalmos, congenital cataract and ectopia lentis, is well known. A developmental defect affecting the optic nerve, with the formation of a hole, is shown in figure 1. Similar anomalies may account for congenital and possibly hereditary involvement of the optic nerve. That certain dysfunctions, such as congenital nyctalopia and color blindness, which probably have an anatomic basis, are hereditary is well understood, but that many of the ophthalmic abiotrophies are also hereditary is not so clearly indicated by some authors. Retinitis pigmentosa, ocular paralyses, some forms of postnatal cataract, lattice-like and nodular degeneration of the cornea and Leber's atrophy of the optic nerve may be found in several siblings. Amaurotic family idiocy and symmetric pigmentary degeneration of the macula may be observed in several generations. Pathologic investigations reveal no evidence of inflammation, but certain groups of cells degenerate early or later in life. The presence of these degenerations in several generations of the same family seems to rule out exogenous

3. Dragstedt, L. R.: Defect in Body's Use of Fat May Cause Artery Hardening, paper read at the meeting of the National Academy of Sciences, Madison, Wis., 1941, Science News Letter **40**:261, 1941.

4. Crisp, W. H.: Senility and the Eye, Am. J. Ophth. **17**:541, 1941.

5. Stieglitz, E. J.: Aging as an Industrial Health Problem, J. A. M. A. **116**:1383 (March 29) 1941.

toxins and vitamin deficiencies and as yet they have not been successfully linked with internal secretion. Some tissues, in which the vital force is low, may succumb earlier than they would if toxins were not present. Apparently the only method of treating the abiotrophies is to attempt to increase local circulation, see that the blood provides an adequate supply of nutrient materials and eliminate any known toxins or raise the resistance to them.

MacCallum [6] has stated: "With the advance of age, wasting becomes evident in many organs, if not in all, although the inconstancy with which

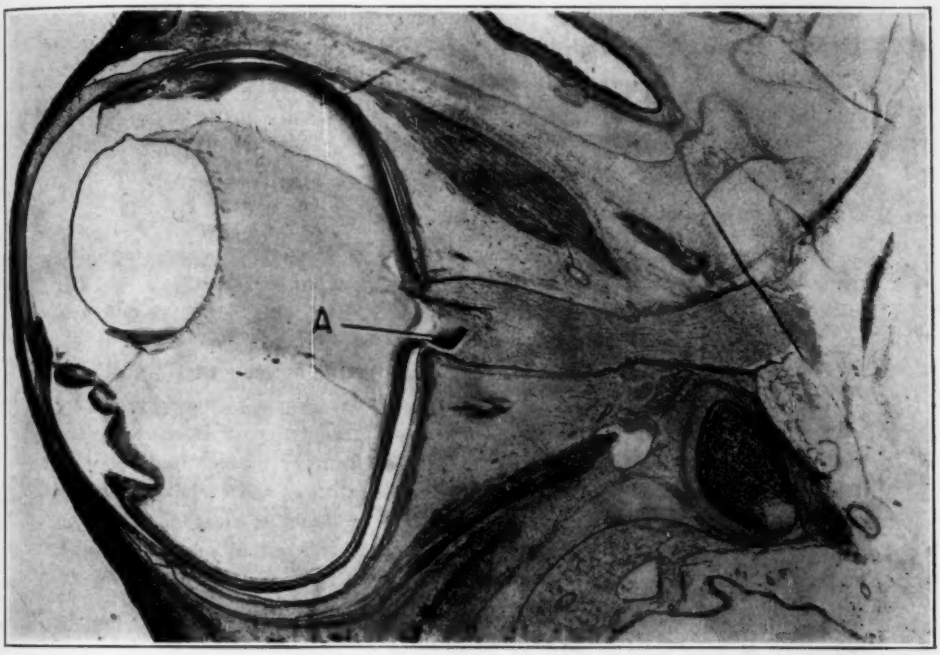

Fig. 1.—Hole in the optic nerve in a 61 mm. human embryo. Similar lesions may account for congenital and possibly hereditary involvement of the optic nerve. *A*, retinal elements replacing nerve fibers.

it appears leads one to wonder whether other factors play a part." Diet could be a factor, and Bain [7] declared that the United States must work harder to feed its babies now, to have well nourished adults in 1961.

Many senile ocular changes are not characterized by pronounced functional disturbances. Among these changes are gradual loss of luster

6. MacCallum, W. G.: Text-Book of Pathology, ed. 3, Philadelphia, W. B. Saunders Company, 1925.

7. Bain, K.: What Babies Eat Now Affects Adult Nutrition in 1961, Science News Letter **40**:277, 1941.

of the cornea; arcus senilis; shallowing of the anterior chamber; decreased motility of the pupil; increased internal dispersion with a yellowish tinge of the lenticular nucleus; colloid deposits on Descemet's membrane, on the anterior lens capsule and on Bruch's membrane; decreased transparency of the vitreous humor, and fluid vitreous with detachment.

GENERAL CONSIDERATIONS

There seems to be little question that faulty circulation and degeneration, the result of vascular changes, cause many of the serious visual disturbances of adults often attributed to age. According to Rones [8] the impaired nutrition resulting from decreased blood supply is responsible for the deposition of fat globules in the various structures.

In discussing lipoid histiocytosis, Heath,[9] reasoning from his fundamental researches, said that it is possible to classify more accurately a considerable variety of ophthalmic lesions through more, though incomplete, knowledge of the humoral and cellular elements involved. He stated:

> By histiocytosis are meant the immune reactions of an intermediate metabolic tissue having properties of phagocytosis prominent in inflammation. . . . The histiocytes are not transient as the leukocytes are. The initial inflow is defensive and protective, but potentially overwhelming and harmful. The mobilizations and hyperplasias of the histiocytes lead to the formation of nonmalignant granulomas.
>
> There are many kinds of initiating lesions. . . . Some of these factors are congestion and stasis in circulation, hemorrhage, precipitation of lipids, angiomatosis, the chemistry of an aging process, free pigments, repeated trauma, circulating chemicals such as phosphorus, endocrine disturbances and chronic infections, particularly tuberculosis and syphilis. By lipid is meant a class of fatty and fatlike substances insoluble in water (except soaps) and put in solution by such solvents as ether, chloroform and alcohols.

Heath called attention to the following conditions, often observed in old eyes, as possibly associated with lipid histiocytosis, some of which have been produced experimentally by feeding animals diets high in fat: 1. Juvenile and familial macular degenerations, which apparently show more chronic storage phenomena with similar basic characteristics. 2. Gaucher's splenohepatomegaly, which often shows deposits of the modified xanthomatosis type in the conjunctiva, cornea and sclera and is a rare form of a still less diffused primary reticular storage of lipin. 3. Xanthomatosis of the skin of the eyelids, which is of two main

8. Rones, B.: Senile Changes and Degenerations of the Human Eye, Am. J. Ophth. **21**:239, 1938.

9. Heath, P.: Ocular Lipid Histiocytosis and Allied Storage Phenomena, Arch. Ophth. **10**:342 (Sept.) 1933.

forms. The nodular, comparatively acute form, is associated with disturbances in sugar metabolism. This lesion can be controlled by diet and exercise. The flat form is more purely a storage phenomenon in older patients. 4. Xanthoma, which is seen in both the bulbar and the palpebral conjunctiva. 5. The gerontoxon, or arcus senilis, which is purely a process of lipid storage and easily produced experimentally. 6. Fibroblastic lipid masses, which frequently are part of chronic infections of the cornea, such as chronic ulcers or old, deep scars. 7. Xanthomatosis of the cornea, which according to biomicroscopic observation is a deep stromal lipochrome and crystalline storage. 8. Asteroid hyalitis, in which the vitreous is the recipient of soap deposits, and synchysis scintillans, in which it is the recipient of numerous cholesterol crystals. 9. Experimental drusen in the choroid of animals on a diet high in fat. 10. Angiosclerosis, circinate retinitis and albuminuric neuroretinitis, which histopathologically show the relative importance of foreign body cellular reactions. 11. Arteriosclerosis with exudation, which has frequently been demonstrated as a focus of fat, especially in the retina.

Little seems to be known concerning the cause or causes of arteriosclerosis, which Dragstedt [8] said is not a necessary part of the aging process, since it does not develop in all people. Dragstedt stated the belief that arteriosclerosis may be a fat disease in the way that diabetes is a sugar disease. In dogs and possibly in human beings, the failure of the pancreas to produce a hormone called lipocaic disturbs the utilization of fat, and arteriosclerosis results. In discussing Dragstedt's research, Oppenheimer [10] suggested that atherosclerosis would have been a better term to use, as excess of lipoids in the blood may lead to atherosclerosis but probably not to arteriosclerosis.

ORBIT AND ADNEXA

In senility the eye seems to become smaller. Hippocrates said that many old persons became "hollow eyed." This appearance is probably caused by a reduction in the amount of orbital fat and slight drooping of the eyelids, and contraction of the pupil probably makes the eye appear smaller.

EYELIDS

The levator of the eyelid becomes weakened, resulting in slight ptosis. Ptosis may be sufficient to interfere with vision.

The cutaneous changes affecting the eyelids include thinning, loss of elasticity, smoothening and folding. The thickness of the skin diminishes because of the reduction in fat and muscle. The skin becomes wrinkled, and the skin below the lower eyelids becomes baggy.

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10. Oppenheimer, B. S.: Personal communication to the author.

Blepharochalasis is commonly observed and in some patients seems to be related to mild repeated attacks of allergic blepharitis associated with sinusitis or other chronic infection. Blepharochalasis has been recognized in later life in persons who have had swelling of the eyelids and an atrophic appearance of the skin since early youth.[11] Senile ectropion and epiphora are often seen in elderly patients. Slight eversion of the punctum is frequently the cause of epiphora, and light cauterization of the conjunctiva will often restore normal relations (fig. 2). The type of senile spastic entropion observed a few months before death has recurred in 3 patients in spite of injections of alcohol, Ziegler punctures and transplantation of the orbicularis oculi muscle.[12] According to Hartmann, the Poulard[13] operation is successful in the treatment of this condition.

The complaint of heaviness of the eyelids and inability to raise them, especially in the morning, is common in elderly persons. The causes are

Fig. 2.—Cauterization of the conjunctiva for eversion of the puncta. *A,* **area to be cauterized.**

varied, and weakness of the levator is usually the result of senile atrophy, although sinusitis, other chronic infections and myasthenia gravis should be excluded. Blepharochalasis causes extra weight, and excision of the redundant skin is beneficial. Chronic meibomianitis, which is sometimes a factor, may be relieved by expression.[14]

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11. Benedict, W. L.: Blepharochalasis, J. A. M. A. **87**:1735 (Nov. 20) 1926.

12. Wheeler, J. M.: Spastic Entropion Correction by Orbicularis Transplantation, Tr. Am. Ophth. Soc. **36**:157, 1938. Meek, R. E.: An Operation for Spastic Entropion, Arch. Ophth. **24**:547 (Sept.) 1940.

13. Poulard, A.: Entropion d'origine angulaire externe traitement chirurgical, Ann. d'ocul. **172**:97, 1935.

14. Berens, C.: A Spatula of Plastic Material for Expressing Meibomian Glands, Am. J. Ophth. **25**:455 (April) 1942.

EXTRAOCULAR MUSCLES

Although senile paralysis of the external muscles of the eye has been mentioned,[15] I have never seen a patient in whom the paralysis was attributable solely to the changes of age.

The near point of convergence is usually more remote in elderly persons, and arteriosclerosis and absorption of toxins from chronic infections probably cause some of the weakness of convergence. In a study of 100 private patients over 60 years of age, the average near point of convergence to the intercentral base line was 113 mm. In a previous study[16] the average near point of convergence to the intercentral base line of 218 men whose average age was 26.64 years was 58.32 mm.

CONJUNCTIVA

The conjunctiva in senile patients shows atrophy of the subepithelial connective tissue, with hyalinization, disappearance of the elastic tissue fibers and increased thickness of the epithelium with a tendency toward keratinization. The entire conjunctiva becomes progressively less elastic with age, so that surgical manipulation is difficult, and pigmentation may appear near the limbus. The conjunctiva commonly becomes thicker and assumes a yellowish color on each side of the cornea in the palpebral fissure.

Pinguecula is stated to be caused by hyaline degeneration and a local hypertrophy of the elastic tissue fibers.[17]

TENON'S CAPSULE

Tenon's capsule reacts to age in much the same way as the conjunctiva. It becomes thicker and less elastic and is subject to fatty changes.

SCLERA AND SCHLEMM'S CANAL

The sclera thickens, becoming more rigid and yellowish. Salzmann[18] stated that "the whole tunica fibrosa undergoes a certain degree of fatty degeneration," but Rones[8] described a fatty infiltration and stated the belief that the equatorial region is only slightly involved.

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15. Wilmer, W. H.: Diseases of the Eye in Old Age, Arch. Ophth. **1**:42 (Jan.) 1929.

16. Wilmer, W. H., and Berens, C.: The Eye in Aviation: Aviation Medicine in the A. E. F., Washington, D. C., Government Printing Office, 1920, p. 182.

17. Fuchs, E.: Zur Anatomie der Pinguecula, Arch. f. Ophth. **38**:143, 1891. Sgrosso, P.: Sulla morfologia e sulla struttura varia della pinguecula, Lavori d. clin. ocul. d. r. Univ. di Napoli **4**:119, 1895. Hübner, W.: Der Lidspaltenfleck, Arch. f. Augenh. **36**:70, 1897-1898.

18. Salzmann, M.: The Anatomy and Histology of the Human Eye, translated by E. V. L. Brown, Chicago, University of Chicago Press, 1912, p. 211.

A peculiar senile degeneration of the sclera in the form of a dark, dirty gray band at the point of attachment of the rectus muscles has been observed by Pillat.[19] In this area the sclera is more translucent, and the condition should be differentiated from senile fatty degeneration and senile spontaneous necrosis.

According to Theobald [20] the inner canals (which Sondermann found in persons between 15 and 70 years of age), the canal of Schlemm and the external canals narrow during the first years of life and widen in old age. The fibers of the pectinate ligament which form the inner wall of Schlemm's canal thicken and sclerose (fig. 3).

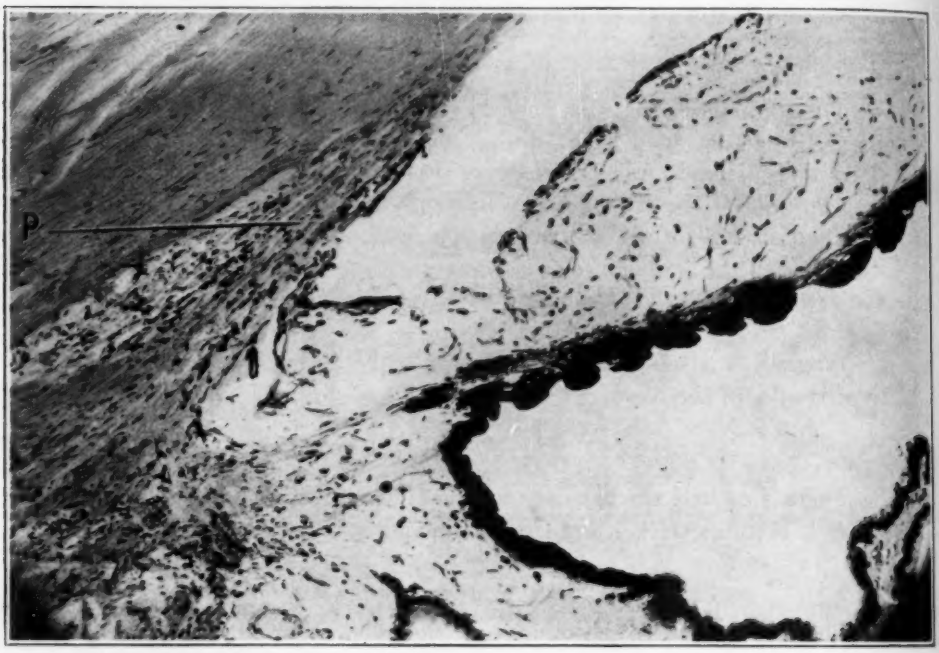

Fig. 3.—Section of Schlemm's canal showing fibrosis and pigmentation of the pectinate ligament (magnification approximately 158; specimen supplied by Dr. Georgiana Theobald.) *P*, pectinate ligament.

CORNEA

Corneal changes with age include diminishing of the apparent diameter of the cornea, loss of luster and transparency, flattening and changes in corneal astigmatism. In the dog as well as in man, the refrac-

19. Pillat, A.: Ueber eine eigenartige senile Entartung der Lederhaut an den Ansatzstellen der geraden Augenmusklen, Ztschr. f. Augenh. **82**:113, 1933.

20. Theobald, G. D.: Schlemm's Canal: Its Anastomoses and Anatomic Relations, Tr. Am. Ophth. Soc. **32**:574, 1934.

tion of the cornea grows less with age.[21] Vogt [22] has mentioned the increase in the internal reflection of the cornea at a level with Descemet's membrane.

Corneal sensitivity increases slightly up to the age of 50; from then on it decreases rather rapidly, to reach a minimum in old age.[23]

Arcus senilis, although sometimes seen in young persons, is more frequent in old age.

"Senile marginal atrophy" has been described by Fuchs.[24]

Thickening and protuberances occur in Descemet's membrane with age. Colloid deposits on Descemet's membrane are frequently seen in the aged. The slit lamp may reveal cornea guttata.

Stähli's line may result from deposition of pigment dust on the posterior corneal surface of senile persons. Krukenberg's spindle and Türk's line have also been observed. According to Duke-Elder,[25] Krukenberg's spindle is merely the accentuation of a general atrophic process in which pigment derived from the uveal tract is deposited on the corneal endothelium and aggregated into the space of an approximately vertical spindle, although minute examination frequently shows that a much larger area of the cornea is bespeckled to a lesser degree.

Band-shaped opacities of the cornea sometimes develop in elderly persons.

ANTERIOR CHAMBER

The anterior chamber tends to become more shallow with age. The posterior chamber also decreases in size.

According to Troncoso [26] pigment is found in the angle of the anterior chamber as a senile condition, as a result of degeneration of the uveal tract and in glaucoma. I have long considered that in many instances the mobilization and deposition of pigment is probably a mild toxic inflammatory process. The frequency with which evidence of a past iritis is found in elderly persons with no history of inflammation and the

21. Kistler, R.: Untersuchungen über die Refraktion von 105 Hunden mit Bermerkungen über senile Veränderungen des Hundeauges, Klin. Monatsbl. f. Augenh. **80**:188, 1928.

22. Vogt, A.: Atlas der Spaltlampenmikroskopie des lebenden Auges; Berlin, Julius Springer, 1921.

23. Zobel, H.: Die Sensibilität der Hornhaut in den verschiedenen Lebensaltern, Arch. f. Ophth. **139**:668, 1938.

24. Fuchs, E.: Lehrbuch der Augenheilkunde, ed. 15, Leipzig, Franz Deuticke, 1926.

25. Duke-Elder, W. S.: Textbook of Ophthalmology, St. Louis, C. V. Mosby Company, 1938, vol. 2, p. 2036. Edgerton, A. E.: Krukenberg's Spindle, Arch. Ophth. **3**:599 (May) 1930. Friedman, B.: Krukenberg's Spindle, a Fusiform Pigmentation of the Cornea, ibid. **1**:590 (May) 1929.

26. Troncoso, M. U.: Gonioscopy and Its Clinical Applications, Am. J. Ophth. **8**:439, 1925.

high incidence of mild iritis following operations for simple glaucoma seem to favor this contention. Chronic nasal catarrh and bronchitis, so commonly observed in elderly persons, sometimes associated with secondary intestinal infection, may be sources of this quiet endotoxic iritis.[27]

IRIS

The entire iris becomes thinner and more rigid. The pupils of the aged become smaller and less mobile, and the color of the iris becomes lighter. In the eighth decade, the border of the pupil, where the pigment has disappeared, looks homogeneous, resembling a glass membrane.

Biozzi [28] has observed two systems of stripes in the ectodermal stratum of the iris which were senile changes. According to Kinney [29] there is but slight relationship between the depigmented circles in the iris (arcus senilis iridis), the patient's age and the degree of arterial or general sclerosis. To speak of the condition as depigmented circles of the iris would be better.

The pathologic changes which probably account for most of the clinical signs observed in old eyes include hypertrophy of the connective tissue fibers, hyalinization of the iris stroma, sclerosis of the blood vessels, atrophy of the cells and migration of the pigment granules in the pigmented epithelial layer.

CILIARY BODY

The ciliary body and iris degenerate in a similar manner. The connective tissue thickens. The function of the ciliary muscle probably lessens to some extent as a result of the observable pathologic changes, but the increased inertia of adjustment of accommodation [30] and the recession of the near point seem to be caused mainly by changes in the lens. Courtney [31] stated the belief that regardless of how little effect the ciliary muscle can have on the crystalline lens, it does continue to try to exert some influence, thereby producing as much discomfort as if it were actually molding the lens.

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27. (*a*) Berens, C.; Nilson, E. L., and Chapman, G. H.: Iritis Produced in Rabbits' Eyes by the Intravenous Injection of Crude and Purified Cultures of Bacteria Isolated from Patients with Certain Inflammatory Eye Diseases, Am. J. Ophth. **19**:1060, 1936. (*b*) Berens, C., and Nilson, E. L.: Ocular Conditions Associated with Coliform Bacteria, Arch. Ophth. **26**:816 (Nov.) 1941. (*c*) Berens, C.; Angevine, D. M.; Guy, L., and Rothbard, S.: Eye Lesions in Experimental Infections: Special Reference to Arthritis, Am. J. Ophth. **21**:1315, 1938.

28. Biozzi, G.: Neuer Spaltlampenbefund in Bereich des Irishinterblattes, Klin. Monatsbl. f. Augenh. **94**:646, 1935.

29. Kinney, V. C.: Arcus Senilis, Internat. J. Med. & Surg. **40**:152, 1927.

30. Ferree, C. E., and Rand, G.: Intensity of Light in Relation to the Near Point and the Apparent Range of Accommodation, Am. J. Ophth. **18**:307, 1935.

31. Courtney, R. H.: Care of Eyes in Old Age, South. Med. & Surg. **100**:124, 1938.

Among the pathologic changes which seemingly account for the functional disturbances of the ciliary body are the following ones: The fibers of the ciliary muscle become thinner and the nuclei fewer, and there is an increase in the connective tissue between the fibers. The interfibrillar tissue becomes hyalinized and involves the muscle fibers as well.

The ciliary processes become elongated and apparently are more numerously branched.[8] The cellular connective tissue of the stroma of the ciliary processes becomes more dense and the cells less numerous. The vessels show signs of sclerosis, the walls becoming thick, fibrosed or hyalinized and the lumens contracted.

The epithelial layer covering the ciliary body and its processes undergoes hyperplasia, forming small and irregular elevations.[8] The cells become convex toward the vitreous, and neighboring excrescences form a festoon-like arrangement, often with a central lumen; in this manner large cystic spaces may be produced.[32] The pigmented epithelium sometimes participates in the proliferation.[33]

In apparently normal eyes the basal hyaline membrane thickens with age and the outer part becomes granular. Cysts of the ciliary body were described by Kuhnt [33a] as senile changes in 1881. In old glaucomatous eyes and after cyclitis atrophic changes are common.

CHOROID

The choroidal blood vessels are particularly affected in age. The walls of the vessels of the choriocapillaris become thickened. Hyaline degeneration may occur, often in patches, and sometimes results in complete obliteration of the vessel. The larger vessels, especially the arteries, show varying degrees of degeneration (fig. 4). Histologically, the choroidal blood vessels may show the following changes: The endothelium of the intima contains fatty globules, and the media and the adventitia become thickened and striated. The muscular coat undergoes changes, partly of a fatty nature, and is replaced by fibrous tissue. The entire vessel wall may become hyalinized, the lumen being markedly restricted or even obliterated. The elastic tissue persists longest and increases in amount, as has been shown by Parsons with specific elastic tissue stains. Choroidal sclerosis in elderly persons disturbs the nutrition of the adjacent tissues, especially the outer layers of the retina.

The pigmented epithelium is one of the first structures to be affected by decreased circulation. Depigmentation and atrophy of the pigmented epithelium occur, permitting the vessels of the choroid to be seen clearly.

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32. Parsons, J. H.: The Pathology of the Eye, London, Hodder & Stoughton, 1904, vol. 1, p. 357.

33. (*a*) Kuhnt, H.: Ueber einige Altersveränderungen im menschlichen Auge, Klin. Monatsbl. f. Augenh. **19**:38, 1881. (*b*) Kerschbaumer, R.: Ueber Altersveränderungen der Uvea, Arch. f. Ophth. **34**:16, 1888.

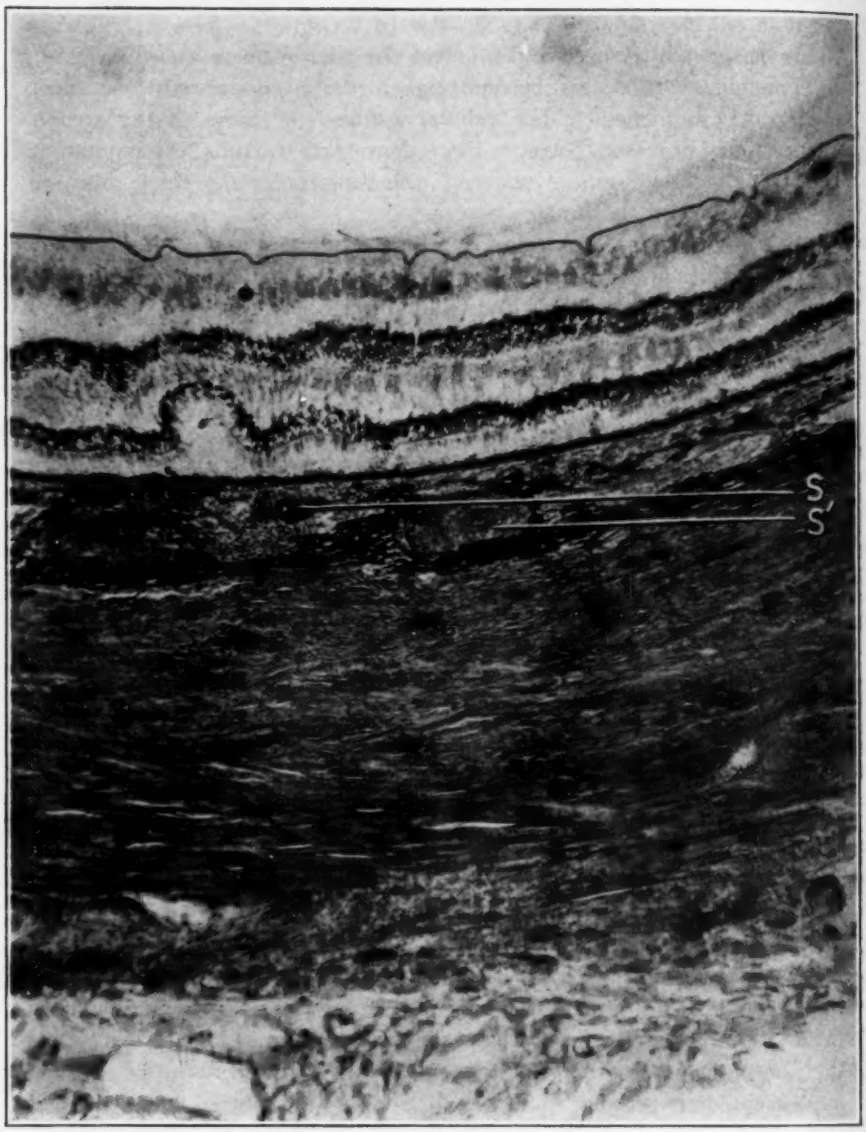

Fig. 4.—Pronounced sclerosis of the choroidal vessels in a patient with nephritic retinopathy (× 200; specimen supplied by Dr. E. B. Burchell). *S* and *S'*, sclerosed vessels.

Hyperplastic changes in the pigmented epithelium are often observed before the atrophic changes, being most pronounced in the anterior portion. These changes are revealed by the proliferation of some of the cells, many of which contain two nuclei; by the formation of colloid bodies, and by uneven thickening of Bruch's membrane.

Drusen appear as sharply circumscribed grayish yellow areas with pigmented borders and are most commonly observed in the macular zone or around the papilla. The disk may be involved (see fig. 13). Microscopically, usually after 45 and almost constantly after 50 and in cases of chronic choroiditis, drusen are seen on the inner surface of the membrane of Bruch, covered by irregular, more or less degenerated pigmented epithelial cells. Although drusen are often considered senile changes, the fact that they occur in young persons, sometimes without apparent disturbance of their circulation, suggests that there may be other etiologic factors, possibly toxic.

Choroidosis Centralis Serosa.—Many lesions, usually observed in older patients, which have been diagnosed as retinitis centralis (Asayman, 1898), angiospastic retinitis [34] or disciform degeneration of the macula, are probably of choroidal origin.[35] The term choroidosis centralis serosa has been used to designate lesions at or near the macula which are caused by localized subretinal edema. Blurred central vision, micropsia and transitory hyperopia may be noted with only slight lowering of central visual acuity. Slight elevation of the retina and the presence of a relative scotoma for blue are early signs. Duggan [35] stated the belief that these primary choroidal lesions should be differentiated from the lesions of central angiospastic retinopathy. All substances are possible etiologic factors which by virtue of their presence (e. g., histamine, epinephrine and nicotine) or their absence (acetylcholine, cevitamic acid, some factors of the vitamin B complex and possibly estrogen) can cause either arteriolar spasm or increased capillary permeability or both. Treatment with vasodilators has a sound physiologic basis, and in addition to the nitrites I have used acetylcholine.

LENS

The lens grows throughout life; it may increase as much as 1 mm. in diameter and a little more than that in thickness. The lens margins become rounded. The cuboid cells of the anterior lens capsule become flattened by the pressure of the enlarging lens.

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34. Horniker, E.: Ueber eine Form von zentraler Retinitis auf angioneurotischer Grundlage (Retinitis centralis angioneurotica), Arch. f. Ophth. **123**:286, 1929.

35. Duggan, W. F.: Choroidosis Centralis Serosa, Arch. Ophth. **27**:123 (Jan.) 1942.

The weight of the lenses of infants aged from 2 weeks to 5 months was 0.0953 Gm. according to Clapp.[36] Priestley Smith [37] estimated that the lens between the ages of 20 and 29 weighs 0.174 Gm., while between 80 and 89 it weighs 0.266 Gm.

Biomicroscopy reveals the following lenticular changes in age: Colloid deposits appear on the anterior lens capsule; the internal diffuse reflection of light increases; the surface of the adult (senile) nucleus becomes more apparent and its lamellas more distinct. The posterior surface of the adult nucleus is also subject to these changes. The lens becomes more fluorescent and yellowish. In the posterior layer the slit beam of light becomes dark orange in hue. By reflected light, in the miosis of age the pupil appears yellowish gray.

The gradual dehydration and sclerosis of the lens fibers cause the cortical lens fibers to become practically as sclerosed as the nuclear fibers in advanced age and less plastic.

Senile exfoliation of the anterior lens capsule was observed clinically and histologically by Wiederkehr [38] and Irvine.[39] Five of Wiederkehr's patients presented evidence of glaucoma (glaucoma capsulare, Vogt). The primary change is apparently the development of vacuoles in the lens capsule, which push the lamellas of the capsule apart. Since these capsular fragments are extremely resistant to enzymes, they are likely to block the channels of exit of the aqueous.

The change in the lens most commonly observed in old age is cataract, and little seems to be known of the cause. However, Clapp [40] stated the belief that alterations in, and death of, the capsular epithelium would seem to be a cause rather than a result of the lenticular changes (fig. 5). Jackson [41] questioned that time has a fixed relation as a cause of cataract, since cataract appears at all ages. The crystalline lens ages slowly. Senile cataract occurs as early as 40 years of age, frequently at 50 and most often between 60 and 70, but may not appear until after 80. Some persons, even if they are 100 or more, never have cortical gray cataract. Vogt [22] has estimated that 90 per cent of all persons

36. Clapp, C. A.: A Communication on the Weight of Infants' Lenses and Their Solids, Arch. Ophth. **42**:618, 1913.

37. Smith, P.: Diseases of the Crystalline Lens and Capsule, Tr. Ophth. Soc. U. Kingdom **3**:79, 1883.

38. Wiederkehr, W.: Weiterer Beitrag zur Klinik und in Histologie der senilen Vorderkapselabschilferung an Hand von 18 spaltlampenmikroskopisch und histologisch untersuchten Augen, Arch. f. Ophth. **139**:541, 1938.

39. Irvine, R.: Exfoliation of Lens Capsule (Glaucoma Capsulare): Report of Two Cases on Etiology, Nature and Significance of Condition, Arch. Ophth. **25**: 992 (June) 1941.

40. Clapp, C. A.: Alterations in the Capsular Epithelium in Immature Cataracts, Am. J. Ophth. **25**:437, 1942.

41. Jackson, E.: Influence of Age in Causing Opacity of the Crystalline Lens: Proper Use of the Word "Cataract," J. A. M. A. **31**:698 (Sept. 24) 1898.

over 60 years of age show senile lenticular changes of various degrees. He [42] stated the belief that these changes are dependent on vitality in the protoplasm, which is conditioned by heredity. The time of onset of senile lenticular changes varies in different species, individuals, organs and tissues. So-called senile cataract is also associated with hydrolysis of the lens protein.[15] According to Davis [43] senile cataract is to be regarded as a specific metabolic disease, and the spontaneous development of a cataract is caused by a direct toxic action on the cells and fibers of the lens. It is known that cataract secondary to uveitis may affect one eye only. However, I have observed unilateral cataract in several patients with unilateral sinus disease whose eyes showed no clinical evidence of inflammation.

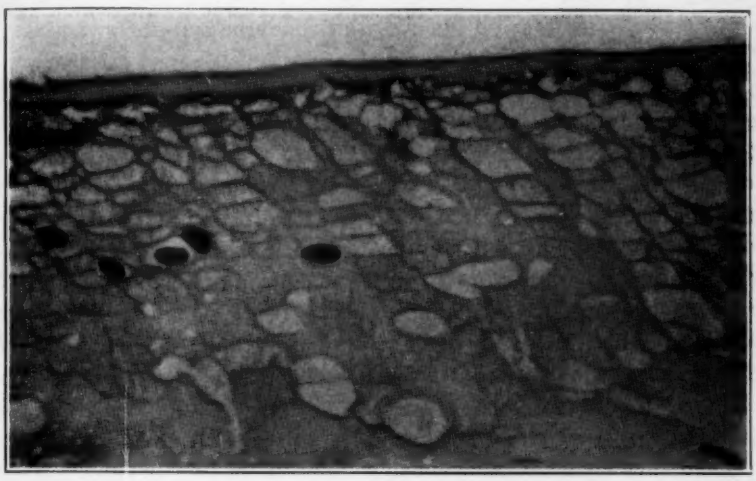

Fig. 5.—Thinning of the capsule and migration of the lens epithelium in a woman aged 70 (from Clapp, C. A.: Tr. Am. Ophth. Soc. **39**:78, 1941).

With age many different kinds of cataract develop. When coronary cataract develops in an elderly patient the local process of senile cortical cataract is required to diminish vision materially, because this form of cataract never progresses to complete opacity of the lens.

The slow calcification of the crystalline lens, with resulting loss of its elasticity, with recession of the near point of distinct vision and with the production of cataract, with advance in age, has been attributed to the combination of the positively charged calcium ions in the lens with the negative phosphate ions to precipitate insoluble calcium phosphate.[44]

42. Vogt, A.: La sénescence de l'oeil, Ann. d'ocul. **172**:106, 1935.

43. Davis, A. E.: Cataract: Its Preventive and Medical Treatment, Philadelphia, F. A. Davis Company, 1937, p. 7.

44. Burge, W. E.; Wickwire, G. C., and Schamp, H. M.: Cause of Calcification of the Crystalline Lens, Arch. Ophth. **17**:234 (Feb.) 1937.

The relation of age and content of the phosphoric acid esters in the lens has been described by Müller.[45] The phosphoric acid esters are difficult to hydrolyze and disappear from the lenses of older animals while those esters which are easily hydrolyzable are still present. Müller stated the belief that it is possible for vitamin C to be formed from these phosphoric acid esters, which are hydrolyzed with difficulty, and that this factor may be of importance in maintenance of the transparency of the lens.

Prevention and Treatment of Pathologic Lenticular Changes.—It is an important question when to tell a patient he has a senile cataract. The problem should be individualized, and if the patient is apprehensive it is advisable to tell a member of the family. If vision is becoming disturbingly affected, it is usually wise to tell even the apprehensive patient that he has a scar on his eye which may be scraped away.

There are no methods of treatment which will cause absorption of lenticular opacities, and Vogt [46] warned against the danger of drawing conclusions from visual acuity in regard to the effects of various therapeutic measures on the progress of cataract. He stated the belief that the apparent success of medical treatment for senile cataract is due to faulty observation. However, Greenwood,[47] after twenty years' experience, said that improvement in the general condition and the use of ethylmorphine hydrochloride have been beneficial. Harkness [48] reported that 50 per cent of the ophthalmologists who responded to a questionnaire claimed that no treatment is helpful, whereas 50 per cent felt that local treatment and general treatment seem to be beneficial in some cases.

Attention to the hygiene of the eye, to the general physical condition (improvement of the blood chemistry, removal of foci of infection), to the diet, to the intake of water (to see that it is sufficient) and to the wearing of glasses which protect the eyes from infra-red rays may have some retarding effect on the development of lenticular opacities. Measures to improve the circulation of the eye and the nutrition of the lens, such as use of solutions of ethylmorphine hydrochloride in increasing doses and hot bathing, may be of benefit. However, I found that lens antigen [49] and ethylmorphine hydrochloride did not seem to retard

45. Müller, H. K.: Ueber die Atersabhängigkeit der leicht und schwer hydrolysierbaren Phosphorsäureester der Linse, Arch. f. Augenh. **110**:128, 1936.

46. Vogt, A.: Des Altern des Auges, Schweiz. med. Wchnschr. **59**:301, 1929.

47. Greenwood, A.: Nonoperative Treatment of Cataract, Tr. Am. Acad. Ophth. **29**:125, 1924.

48. Harkness, G. F.: Incipient Cataract, Am. J. Ophth. **8**:132, 1925.

49. Berens, C., in discussion on Wheeler, J. M.: Treatment of Cataract with Lens Antigen, paper presented at the meeting of the Medical Society of the State of New York, May 12, 1927.

the development of cataract, whereas general treatment and the removal of active or potentially active foci of infection did seem to be beneficial, in over 75 per cent of the cases in a control series.

When miosis and rigidity of the pupil are associated with cataract, a device [15] consisting of black rubber (6 by 4 inches, or 15 by 10 cm.), in the center of which there is an aperture (4 by ¼ inches, or 10 by 0.64 cm.), may improve reading ability. Eucatropine hydrochloride, duotone lenses, strong plus lenses (+ 6.00 to + 8.00 D.) and the illumination found to be best by practical tests seem to help patients with certain types of cataract. Optical iridectomy may prove beneficial.

The concentration of cevitamic acid (vitamin C) in the lens decreases with age [50] and markedly in association with cataract. Duke-Elder [51] stated that either the loss of vitamin C is secondary to changes in the lens, probably of the nature of a disturbance in glycolysis, or diminution or deficiency in this vitamin precedes and may determine the formation of cataract.

It has been shown [52] that when a diet deficient in vitamin B_2 (or G) is administered to young rats, cataract of varying morphologic types, cortical, nuclear and diffuse, develops and passes through all stages of development of incipience, intumescence and maturity if the diet is persisted in. In spite of experiments with vitamins C and G, the use of these vitamins has not been proved to be of especial value in the prevention or cure of cataract.

In the removal of cataract my experience agrees with that of Elliot,[53] who stated that he would rather operate on subjects 90 years of age and older than on many who are only in the sixth and seventh decades of life. I have operated on several persons over 90 years of age and on 1 who was 103 years old; all the operations were successful.

Functional Changes in the Lens.—According to Robertson [54] age has a bearing on the speed of adjustment of the eye to clear seeing at different distances. He stated the belief that fatigue also affects the speed of adjustment, at all ages but especially as age progresses.

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50. Müller, H. K.: Kammerwasser und Linsenstoffwechsel, Arch. f. Augenh. **108**:41, 1933.

51. Duke-Elder, W. S.: Textbook of Ophthalmology, Philadelphia, C. V. Mosby Company, 1942, vol. 3, p. 3134.

52. Day, P. L.; Langston, W. C., and O'Brien, C. S.: Cataract and Other Ocular Changes in Vitamin G Deficiency, Am. J. Ophth. **14**:1005, 1931.

53. Elliot, R. H.: Cataract Operation in Extreme Old Age, Brit. M. J. **1**:132, 1931.

54. Robertson, C. J.: Effect of Fatigue on the Adjustment of the Eye to Near and Far Vision, Arch. Ophth. **17**:859 (May) 1937.

The normal color perception for the blue end of the spectrum is reduced with age, probably because of the filtering effect of the yellow tint of the lens.

Refraction.—Brown [55] found that between the ages of 43 and 51 there is a slight yearly increase toward the myopic side, averaging 0.09 D., possibly due to an increase in the index of refraction of the lens. The findings were, respectively, 0.04, 0.03, 0.01, 0.09, 0.02, 0.01, 0.04, 0.08 and 0.08 D. (average, 0.03 D.) of net average increase of refraction for the successive years. A recent restudy of his material showed nearly the same average yearly change (0.04 D.), but he remarked that the material is still too small to permit reliable deductions.[56] Brown [57] has stated:

> My data tend to show that after certain functional refractive states become static, sometime between the ages of 20 and 25, they remain so, practically unchanged, in the average eye for many years, certainly for fifteen or twenty. This is rather remarkable when one considers that a number of variables, such as the length of the eye, the curve of the cornea and the lens and the index of refraction, are involved. The question naturally arises as to how far real pathologic change is responsible for senescence and how much of aging is really only decrease of physiologic capacity.

After 60 years of age there is a tendency toward lower hyperopia and actual and progressive myopia; the result is the so-called second sight of old persons, which enables them to "read without glasses." Although near vision may improve, there are usually coincident loss of distant vision and actual lowering of the visual acuity, and cataracts may develop.[58]

Astigmatism also changes with age, and according to Jackson [59] the average before 25 years of age was 1.04 D. of corneal and 0.61 D. of lenticular astigmatism. After 50 years the average was 1.24 D. of corneal and 0.71 D. of lenticular astigmatism.

Vele [60] stressed the fact that inverse astigmatism often develops and increases with age. Vita [61] has stated that if there is a slight inverse

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55. Brown, E. V. L.: Net Average Yearly Changes in Refraction of Atropinized Eyes from Birth to Beyond Middle Life, Arch. Ophth. **19**:719 (May) 1938.

56. Brown, E. V. L.: Use-Abuse Theory of Changes in Refraction Versus Biologic Theory, Arch. Ophth. **28**:845 (Nov.) 1942.

57. Brown, E. V. L.: Personal communication to the author.

58. Jackson, E.: Changes in Refraction with Age, Am. J. Ophth. **3**:228, 1920.

59. Jackson, E.: Norms of Refraction, J. A. M. A. **98**:132 (Jan. 9) 1932.

60. Vele, M.: Il comportamento dell'astigmatismo corneale inverso con l'età e nella miopia, Boll. d'ocul. **12**:1339, 1933.

61. Vita, A.: Senile Inverse Astigmatism as Contraindication for Use of Spherical Lenses of Meniscus Type in Correction of Presbyopia, Rassegna ital. d'ottal. **4**:622, 1935.

astigmatism, such as would not require correction with cylindric or toric lenses, it is advisable to use biconvex lenses or, eventually, lenses of the meniscus type with weak incurvation (periscopic lenses, base 1.25 D.). His reason is that oblique astigmatism, which occurs when the patient is looking obliquely downward through these glasses, corrects the inverse astigmatism of the eye.

Presbyopia.—It is questionable whether presbyopia should be classified as a senile condition. The changes which cause presbyopia are mainly a lessening of the plasticity of the lens and an increase in its index of refraction. I question whether the ciliary muscle weakens greatly. The increase of the indexes of refraction of the outer layers of the lens (Helmholtz [62]) must produce a decrease of the refracting power of the lens and consequently cause the second focal point of the eye to be moved farther back. Alexander [63] contended that the cause of the diminution of the power of the lens as age advances is the diminution in the convexity of its surface and in the surfaces of the nucleus from their growth.

I agree with Sudranski [64] that homatropine is valuable for the more optically precise refraction in many cases of presbyopia. I prefer disks of homatropine hydrobromide and cocaine hydrochloride (1/50 grain [1.3 mg.] of each) and believe that the cycloplegic findings are helpful in checking of the postcycloplegic acceptance. If physostigmine salicylate (0.5 per cent solution) is used to contract the pupil, the procedure is practically without danger, but the tension should be determined before the cycloplegic is instilled and after the pupil is dilated.

The presbyopic patient requires more light in order to read, and the majority of persons with cataract need the increased light afforded by a larger pupil.

Illumination and Old Eyes.—According to Ferree, Rand and Lewis [65] there is a much greater need of the higher intensities of light for old than for young eyes. They gave the following reasons: "Smaller pupil; inferior imaging power of the refracting media; diminished transparency of the media; the decay in all its processes of adaptation and

62. Helmholtz, H.: Helmholtz's Treatise on Physiologic Optics, edited by J. P. C. Southall, Ithaca, N. Y., The Optical Society of America, 1924, vol. 1, p. 139.

63. Alexander, G. F.: Age Changes in the Refraction of Crystalline Lens, Am. J. Ophth. **4**:676, 1921; Tr. Ophth. Soc. U. Kingdom **41**:219, 1921.

64. Sudranski, H. F.: Relation of Dynamic to Static Refraction in Presbyopic Patients Forty Through Fifty Years of Age, Arch. Ophth. **23**:545 (March) 1940.

65. Ferree, C. E.; Rand, G., and Lewis, E. F.: The Effect of Increase of Intensity of Light on the Visual Acuity of Presbyopic and Non-Presbyopic Eyes, Tr. Illum. Engin. Soc. **29**:296, 1934.

adjustment and the failing powers of the retina itself." They stated the belief that without question age is the most important factor in the effect of intensity of light on clear seeing and the grading of intensity to meet the age requirement is the major problem in the use of intensity in lighting practice. Some of the investigations carried out by me and my associates [66] concerning illumination would seem to confirm the opinion of these workers.

In a study of the intensity of light in relation to the near point and the apparent range of accommodation, Ferree and Rand [67] stated that in general an increase of intensity of light greatly improves vision at any distance (table 1). It may be seen from table 1 that increased

TABLE 1.—*Effect of Increased Intensity of Illumination on the Near Point (Ferree and Rand* [67]) *

Intensity of Illumination, Foot Candles	Emmetropic Observer, M. S., Aged 23; Type Read No. 15		Observer G. R., Aged 44, with Corrected Myopia; Type Read No. 15		Presbyopic Observer, A. G., Aged 52; Type Read No. 50	
	Near Point, Cm.	Apparent Diopters of Accommodation	Near Point, Cm.	Apparent Diopters of Accommodation	Near Point, Cm.	Apparent Diopters of Accommodation
0.5	10.35	9.66	25.8	3.88	61.0	1.64
0.75	10.04	9.96	22.4	4.46	58.0	1.72
1.0	9.82	10.18	21.2	4.72	51.0	1.96
2.5	9.72	10.29	19.9	5.03	42.5	2.35
5.0	9.64	10.37	18.8	5.32	39.0	2.56
10.0	9.56	10.46	17.6	5.68	36.0	2.78
15.0	9.45	10.58	17.1	5.85	34.5	2.90
20.0	9.40	10.64	16.8	5.95	32.5	3.08
25.0	9.35	10.70	16.6	6.02	31.0	3.23
37.5	9.30	10.75	16.4	6.10	28.5	3.51
50.0	9.24	10.82	16.25	6.15	27.5	3.64
75.0	9.14	10.94	16.0	6.25	24.5	4.08
100.0	9.04	11.06	15.8	6.33	22.5	4.44

* Test object, Bausch & Lomb reading card.

illumination causes a substantial approach of the near point to the eye, which is especially marked in old eyes. Experiments made in association with Dr. S. B. Sells have so far shown only slight differences between presbyopic and nonpresbyopic groups of clinic patients when time was permitted for adaptation to the different intensities of illumination and examinations were made on different days. However, even with this method of study the near point is more affected in the presbyopic subjects than in the nonpresbyopic subjects. Higher intensities of light

66. McFarland, R. A.; Knehr, C. A., and Berens, C.: Metabolism and Pulse Rate as Related to Reading Under High and Low Levels of Illumination, J. Exper. Psychol. **25**:65, 1939.

67. Ferree, C. E., and Rand, G.: Intensity of Light in Relation to the Near Point and the Apparent Range of Accommodation, Am. J. Ophth. **18**:307, 1935.

sometimes may be used as senility approaches to defer the constant use of reading glasses and in the earlier stages of presbyopia to lessen the need of frequent changes in the strength of the glasses.

VITREOUS

Rarefaction and shrinking of the fibrillae of the vitreous have been observed in the aged.[68] According to Vogt [22] the senile framework shows increased luminosity and the tunic-like vertical folds especially are visible and bright.

Isakowitz [69] observed a bilateral senile ring formation in the vitreous humor of a patient 57 years of age.

Senile forms of synchysis scintillans have also been observed by Joubert,[70] who claimed that continuous galvanization produces satisfactory and rapid results in synchysis scintillans but vision may not be recovered. Other senile changes are decreased transparency of the vitreous humor and a fluid vitreous with detachment.

RETINA

In the aged the retina loses its transparency and luster. A localized tessellated appearance is caused by diffuse or circumscribed atrophy affecting the pigmented epithelium.

After the fourth decade, the frank inflammatory conditions observed in the earlier decades of life are less frequent, but insidious inflammation and degenerations, which are often without subjective symptoms, are more common and may develop unnoticed by the patient.[71]

Retinal Degeneration and Central Senile Chorioretinitis.—Terrien [72] stated the belief that destructive vascular lesions in the retina are rarer in old persons than in other age groups, but he stressed the frequency of cystic degeneration of the retina in the extreme periphery (fig. 9 *B*) and of macular lesions in the aged.

The retinal lesion usually described as senile macular degeneration, Fuchs named central senile retinochoroiditis. This lesion is of great importance because it destroys central vision and may make reading impossible.

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68. Addario, C.: L'involuzione senile del vitreo a della sua matrice ciliare, Internat. Cong. Ophth., 1905, sect. B, p. 190.

69. Isakowitz: Beiderseitige frisch entstandene ringförmige Glaskörpertrübung, Klin. Monatsbl. f. Augenh. **88**:369, 1932.

70. Joubert, L. de G.: Un cas de synchisis scintillant à forme sénile, J. de l'Hôtel-Dieu de Montréal **5**:193, 1936.

71. Zentmayer, W.: Importance of Ocular Examinations After Fourth Decade of Life, Delaware State M. J. **10**:33, 1938.

72. Terrien, F.: Les modifications apportées par l'âge dans le globe oculaire; l'oeil sénile, Paris méd. **12**:517, 1922.

Classification: Four clinical types of central senile chorioretinitis have been described by de Schweinitz [73] (fig. 6). In type I the macula may appear darker than normal, it may be delicately mottled or white glistening dots may be seen (fig. 6 *A*). In type II yellowish white spots in the macula are interspersed with pigment dots and occasionally with hemorrhages. Yellowish white spots at times may represent drusen (fig. 6 *B*). In type III a round or slightly oval hole appears in the macula, first described by Noyes (1871) and most commonly seen after injury to the eyeball (Haab, 1920; fig. 6 *C*). In type IV grayish or greenish heaped exudates, which may resemble tumors and hemorrhages, may be present (fig. 6 *D*). This type has been named senile macular exudative retinitis by Coppez and Danis (1923; fig. 7). Possibly central cystic degeneration should be classified with this type of macular lesions. Central cystic degeneration in association with severe retinitis circinata was observed in a woman 70 years of age (fig. 8). Microscopic sections of the macular region in elderly patients are shown in figure 9.

The diagnosis of early macular changes can be made only after complete dilation of the pupil and careful ophthalmoscopic examination, possibly with red-free light or the Gullstrand ophthalmoscope. The finding of central relative blue or yellow-blue blindness by means of perimetric examination may precede ophthalmoscopic diagnosis.

Pathologic studies have shown degeneration of the neurons and pigmented layer of the retina in the early stages, with involvement of the choroid later. Cystic degeneration of the macula (figs. 8 and 9) may precede the formation of a hole. The absence of angiosclerosis has led to the belief that senile macular chorioretinitis is an abiotrophy.

Treatment: Treatment of central senile chorioretinitis is unavailing according to standard textbooks. Many authors agree with Behr,[74] who said that senile degeneration of the macula is like the congenital, infantile, juvenile, virile and presenile forms, only an especial type of the general clinical aspect of macular heredodegeneration. The cause of the changes, according to Behr, lies, not in the external nocuous influences, but in the genetic units in the parental germ plasm. It is a hereditary premature death of the maculoretinal neuron. However, Heath [74a] stated that "some senile macular deposits are held or progress less rapidly, if the patient is put on a low fat and carbohydrate diet; and the use of thyroid is sometimes useful; also insistence on exercise or massage as a routine is valuable."

There seems to be a question in some cases of macular degeneration whether inflammation is not a factor, as Fuchs's designation of senile

73. de Schweinitz, G. E.: Senile Macular Disease, Atlantic M. J. **31**:818, 1928.

74. Behr, C.: Die Anatomie der "senilen Makula" (der senilen Form der makularen Heredodegeneration), Klin. Monatsbl. f. Augenh. **67**:551, 1921.

74a. Heath, P.: Personal communication to the author.

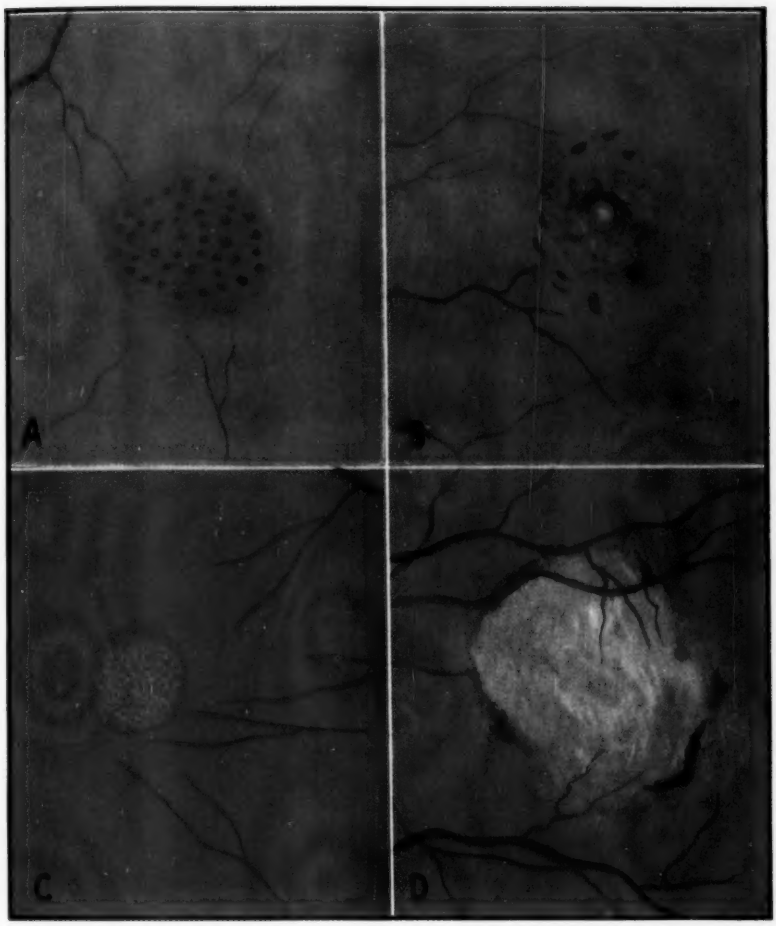

Fig. 6.—Lesions of the macula. *A*, familial degeneration of the macula in a girl aged 10 (similar to senile macular chorioretinitis of de Schweinitz type I). *B*, senile chorioretinitis of the macula with pigmentation and hemorrhages (de Schweinitz type II). *C*, beginning hole in the macula in a late stage of senile chorioretinitis of the macula (de Schweinitz type III). *D*, senile exudative chorioretinitis of the macula (de Schweinitz type IV).

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chorioretinitis would imply. De Schweinitz [75] described various types of so-called senile macular degeneration which had been favorably influenced in the sense of a cessation of crops of small hemorrhages by the elimination of prostatic infection and the administration of autogenous vaccine. However, in no instance did degenerated areas resume function or pigment spots, etc., disappear. He referred to the period when metamorphopsia and relative blue scotomas indicate the beginning of so-called

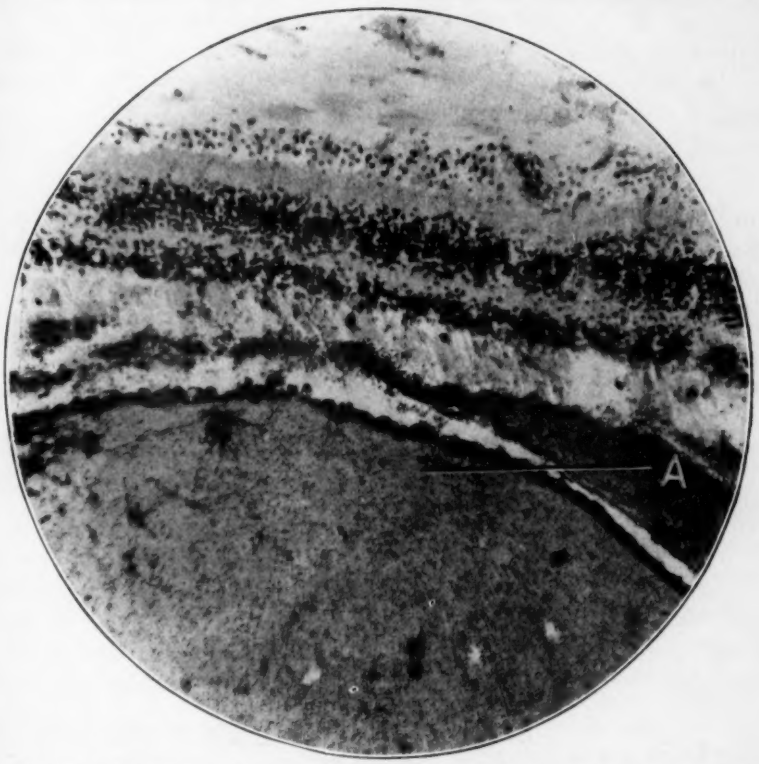

Fig. 7.—Macular region in senile exudative chorioretinitis of the macula (specimen supplied by Dr. E. B. Gresser). *A*, organized subretinal exudate.

senile macular chorioretinitis as the period when the elimination of focal infection in the prostate, teeth or bladder is important to prevent permanent functional loss.

In my experience, chronic hyperplastic sinusitis seems to have been a factor in some cases of senile macular chorioretinitis, but the relation of

75. de Schweinitz, G. E.: Ocular Disorder Probably Due to Prostatic and Bladder Nonvenereal Infection, Am. J. Ophth. **8**:401, 1925.

tonsillar, prostatic and intestinal infection to this condition has been less clear. However, these possible sources of infection should also be considered.[76] Small doses of antigen made up of chemically killed autogenous bacteria [77] seem to be of benefit in improving the general health and possibly in raising local cellular resistance.

Experience has led me to agree with de Schweinitz that treatment should not be abandoned until attempts have been made to improve the local circulation (administration of ethylmorphine hydrochloride, dia-

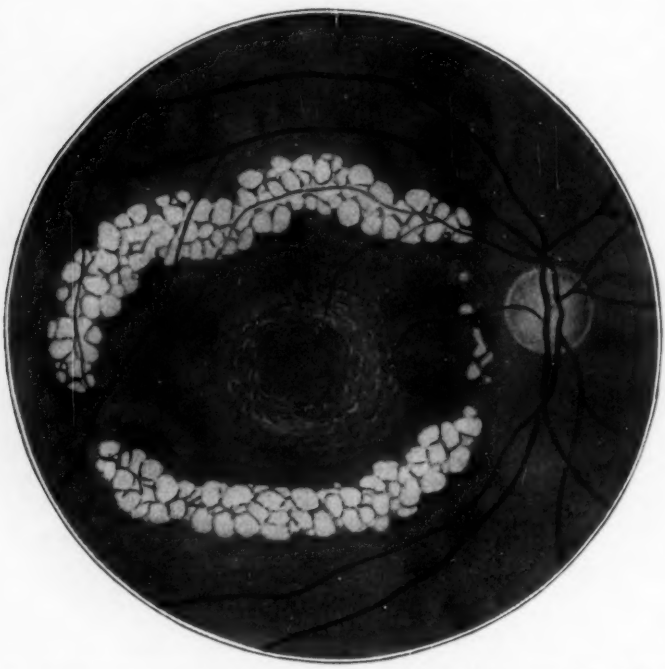

Fig. 8.—Cystic degeneration of the macula with retinitis circinata (Mrs. G. H. S., aged 70, right eye).

76. Berens, C., and Nilson, E. L.: Experimental Acute Iridocyclitis in Rabbits Produced by Coliform Bacteria Isolated from the Upper Respiratory Tract of Man, Am. J. Ophth. **24**:645, 1941. Berens, Nilson and Chapman.[27a]

77. Small, J. C.: Treatment of Rheumatic Carditis in Children, J. Lab. & Clin. Med. **19**:693, 1934. Miller, S. R.: Appraisal of Value of Vaccine Therapy in Chronic Arthritis, South. M. J. **26**:583, 1933. Rawls, W. B.; Gruskin, B. J., and Ressa, A. A.: Intravenous Vaccine Therapy in Chronic Arthritis, Ann. Int. Med. **7**:566, 1933. Stiles, M. H., and Chapman, G. H.: Relationship Between Agglutinability and Certain in Vitro Tests of Staphylococci, Streptococci and Colon Bacilli Isolated from Persons Suspected of Having Chronic Infection, J. Lab. & Clin. Med. **24**:620, 1939. Chapman, G. H., and Berens, C.: Comparison of Intradermal Tests with Agglutinability and Certain in Vitro Tests of Streptococci, Staphylococci,

thermy and use of vasodilators) and the general health. The progress in some cases seems to have been arrested with treatment, but improved vision has rarely been recorded even when the patient was treated as soon as the earliest signs appeared.

My opinion concurs with that of van der Hoeve,[78] who has analyzed his own statistics and those of others to show that a relative antagonism exists between senile cataract and senile macular degeneration. He does not believe that both diseases are the result of the action of ultraviolet rays on tissues which are congenitally less resistant.

Bedell [79] stated the belief that senile pigmentation is an exaggeration of drusen, Tay's choroiditis and senile macular degeneration. He said that benign drusen may become so large and so central as to embarrass the ophthalmologist who does not use the discriminating tests for vision and field defects.

Role of Certain Exogenous Toxic Agents in Senile Retinal Changes.—Indulgences which seem to have little deleterious effect on young tissues and functions, in the aged—because of cumulative action, lower resistance of the tissues or both—may cause functional impairment or serious organic change. Notable among these excesses according to Zentmayer [71] are relatively high intakes of carbohydrate, alcohol and tobacco.

Changes in the retina and optic nerve caused by tobacco and ethyl alcohol are rarely seen before the age of 40.

Retinal Angiosclerosis.—The early recognition of retinal angiosclerosis is important because the retinal vessels are a fairly reliable index of the condition of the cerebral vessels and the arterioles throughout the body. A senile angiosclerosis of the fundus was described by de Schweinitz.[80] According to my observations and those of others,[81] the most dangerous element of hypertensive disease is angiospasm.

Micrococcus Catarrhalis, and Colon Bacilli Isolated from Persons Suspected of Having Chronic Infection, ibid. **24**:601, 1939. Berens and Nilson.[27b] Berens and others.[27c]

78. van der Hoeve, J.: Der Antagonismus zwischen seniler Katarakt und seniler Makuladegeneration (Haab), Ztschr. f. Augenh. **63**:127, 1927.

79. Bedell, A. J.: The Clinical Importance of Pigment in the Fundus, Tr. Am. Acad. Ophth. **41**:446, 1936.

80. de Schweinitz, G. E.: Diseases of the Eye, Philadelphia, W. B. Saunders Company, 1924.

81. Wagener, H. P.: Retinal Vascular Changes in Hypertension, Ann. Int. Med. **4**:222, 1930. Mylius, K.: Funktionelle Veränderungen am Gefäss-system der Netzhaut, Berlin, S. Karger, 1928, p. 82. Aubaret, E., and Sedan, J.: L'angor ocularis, Presse méd. **36**:1139, 1928.

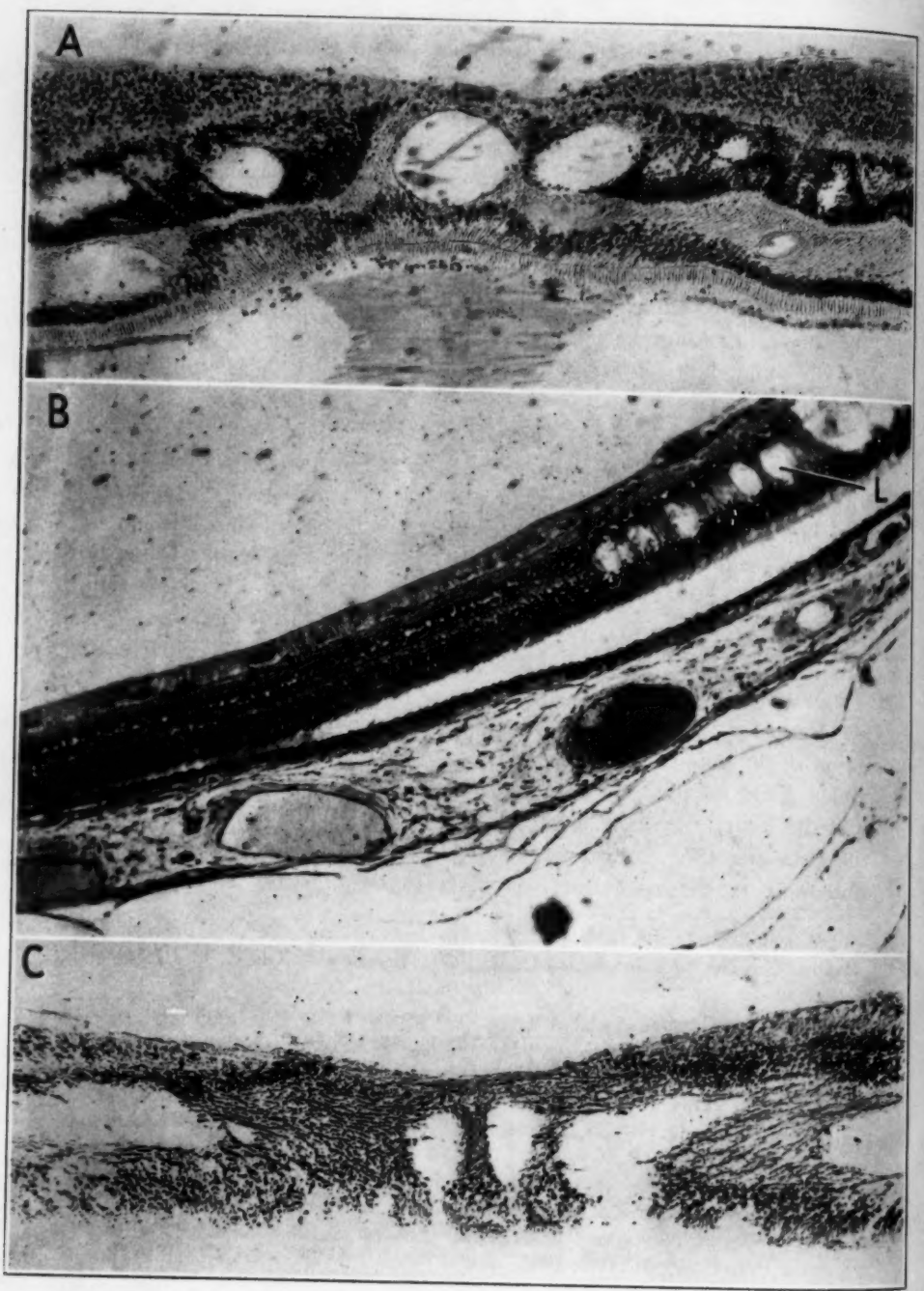

Figure 9

(See legend on opposite page)

Arterial constriction may cause arteriosclerosis and possibly the hypertension. Certainly serious cerebral, retinal and renal complications may result from angiospasm.

Keyes and Goldblatt [82] reported that changes visible with the aid of the ophthalmoscope appeared in the eyes of 8 dogs and 1 monkey after varying periods of experimental hypertension caused by renal ischemia. The retinal arterial vascular system was apparently primarily affected, with or without the appearance of hemorrhages and edema in the retina.

Nephritic Retinopathy.—Only in patients with chronic glomerulonephritis is so-called nephritic retinopathy a condition of later life. Present conceptions of renal retinitis usually include three clinical and pathogenic entities, which may often be differentiated ophthalmoscopically: (*a*) malignant hypertensive neuroretinitis, (*b*) arteriosclerotic retinopathy and (*c*) choked disk caused by increased intracranial pressure from edema of the brain.

Volhard recognized renal arteriolosclerosis without renal insufficiency, essential hypertension for which no cause is known.[83] This condition commonly appears between the ages of 50 and 70. Fishberg and Oppenheimer [84] have added to existing knowledge of the retinal and the renal pathology of so-called hypertensive retinopathy. In their 10 cases of essential hypertension with malignant hypertensive neuroretinopathy in which the patients came to necropsy, necrosis of the renal arterioles was present. On the other hand, necrosis of the renal arterioles was absent in 11 instances of essential hypertension without malignant hypertensive neuroretinopathy that were studied at necropsy (fig. 10).

82. Keyes, J. E. L., and Goldblatt, H.: Experimental Hypertension: IV. Clinical and Pathologic Studies of the Eye; a Preliminary Report, Arch. Ophth. **17**:1040 (June) 1937.

83. Crisp, W. H.: Senility and the Eye, Am. J. Ophth. **17**:541, 1934.

84. Fishberg, A. M., and Oppenheimer, B. S.: The Differentiation and Significance of Certain Ophthalmoscopic Pictures in Hypertensive Diseases, Arch. Int. Med. **46**:901 (Dec.) 1930.

EXPLANATION OF FIGURE 9

Microscopic sections of the macular region and peripheral portion of the retina, showing cystic degeneration. *A*, cystic degeneration of the macula in iridocyclitis (S. G., aged 65; specimen supplied by Dr. I. Mensher). *B*, cystic degeneration of the peripheral portion of the retina in a patient aged 74 (magnification approximately 115; specimen supplied by Dr. E. B. Gresser). *L*, cystic space. *C*, advanced cystic degeneration of the macula in glaucoma (R. K., aged 63; specimen supplied by Dr. I. Goldstein).

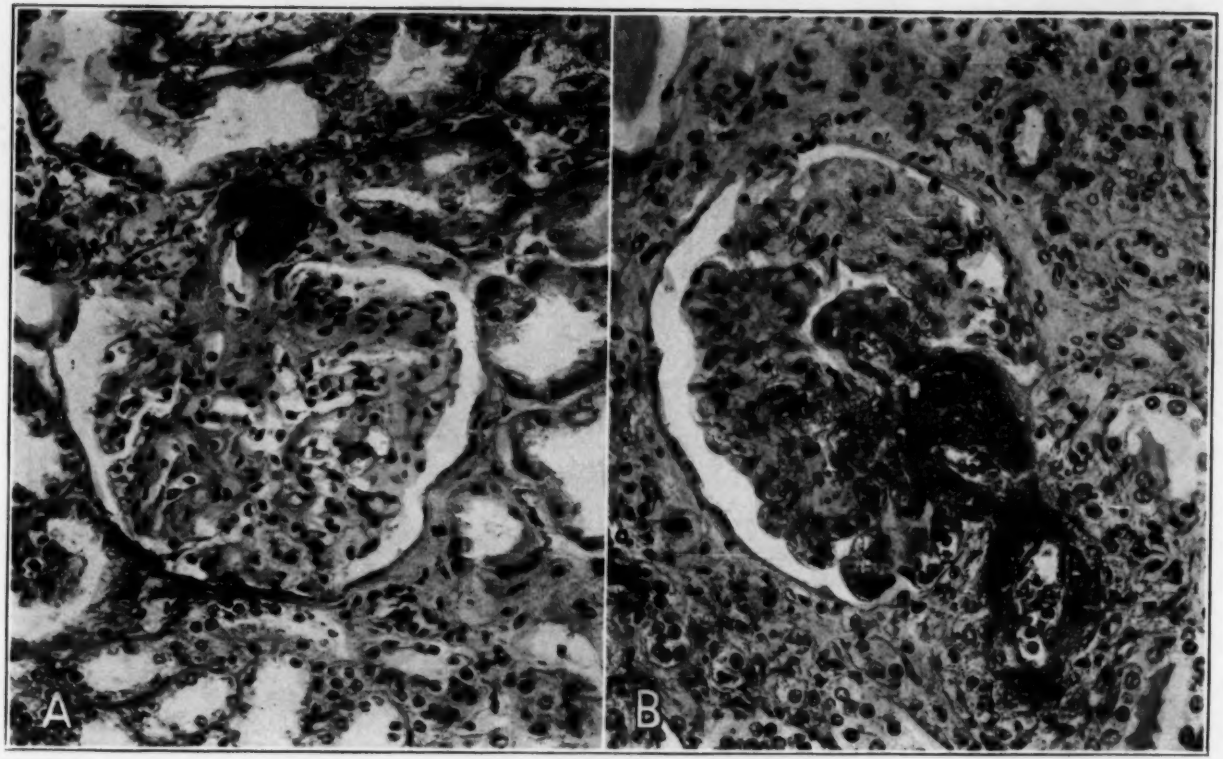

Fig. 10.—Histologic sections of kidneys, illustrating the glomerular lesions in benign and in malignant nephrosclerosis (specimens supplied by Dr. B. S. Oppenheimer and Dr. P. Klemperer). *A*, typical simple hyalinization of the vas efferens. The patient had essential hypertension; the retina was normal. *B*, arteriolar necrosis in malignant nephrosclerosis. The patient had the retinopathy of malignant hypertension.

Diabetic Retinopathy.—The retinal picture in diabetes (fig. 11) seems to bear some relation to senility, because the average age for the occurrence of diabetic retinitis was 55 years as reported by Leber. Ramsay [85] expressed the opinion that this condition is invariably limited to the later years of life. According to Waite and Beetham [86] retinal hemorrhages in diabetic patients multiply with age, and with the continued duration of diabetes, to a degree out of proportion to the age factor, but they show no obvious correlation with sclerosis of retinal vessels, with

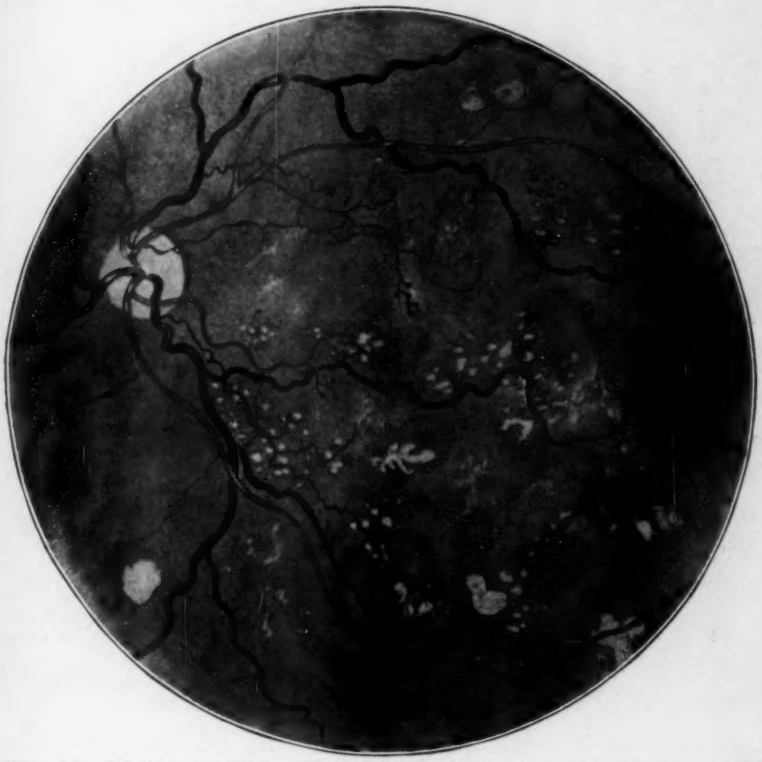

Fig. 11.—Diabetic retinitis. Note telangiectases, tortuosity of the arterioles, indentation of the veins by the arteries, hemorrhages and grayish yellow, irregularly shaped lesions in the retina.

vascular hypertension, with renal disorders, with the dose of insulin or with the level of sugar or of calcium in the blood.

85. Ramsay, A. M.: Some Ocular Manifestations of High Blood Pressure: A Plea for the Routine Use of the Ophthalmoscope in Clinical Medicine, Glasgow M. J. **117**:281, 1932.

86. Waite, J. H., and Beetham, W. P.: The Visual Mechanism in Diabetes Mellitus, New England J. Med. **212**:367, 1935.

However, Elwyn [87] stated that an increase in the blood sugar level results in dilatation of the small vessels with slowing of the blood flow, which deprives the retina of sufficient food and oxygen. Hemorrhages, exudates and deposits of hyaline and of lipoid material usually result from this state of prestasis.

OPTIC NERVE

Partial atrophy of the optic nerve has been observed in the aged. De Schweinitz reported a condition in elderly persons characterized by

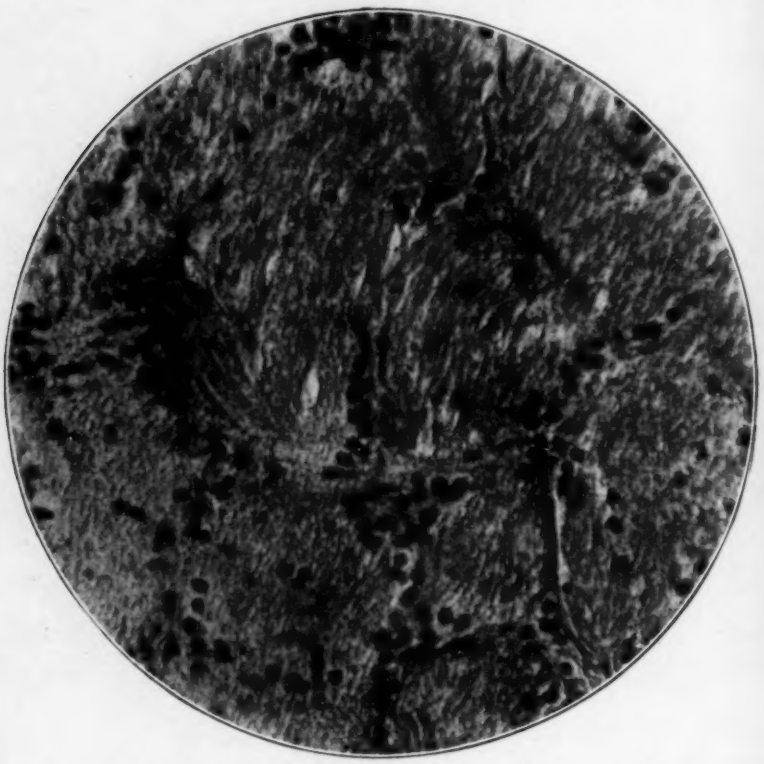

Fig. 12.—Senile atrophy of the optic nerve in senile retinal sclerosis (× 40; specimen supplied by Dr. E. B. Gresser).

atrophic pallor of the optic nerve, without shrinking, sometimes associated with senile retinal sclerosis (fig. 12). The atrophy may result from pressure of the sclerosed carotid artery on the optic nerve. Atrophic pallor of the optic nerve, usually without shrinking, is sometimes associ-

87. Elwyn, H.: The Problem of Diabetic Retinitis, Arch. Ophth. **25**:139 (Jan.) 1941.

ated with retinal arteriosclerosis in elderly persons and with a relative central scotoma. The visual acuity and the central field are only slightly reduced. The scotoma sometimes appears in the winter and often disappears in the summer; apparently in some cases its development is associated with a slight increase in absorption of bacterial toxins from the sinuses. In rheumatic patients the general discomfort often seems to increase and decrease as the relative central scotoma develops and subsides.

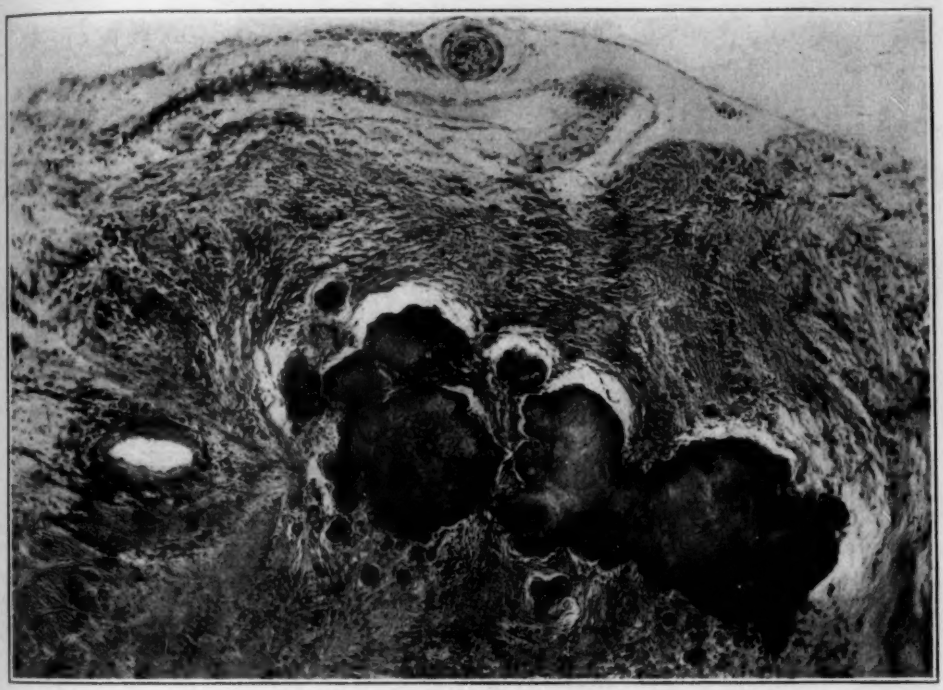

Fig. 13.—Colloid bodies in the optic nerve head in a man 57 years of age (magnification approximately 110; specimen supplied by Dr. E. B. Gresser).

Improvement of optic nerve atrophy with retrobulbar injection of atropine sulfate has been reported by Abadie [88] and by Springovitsch [89] and of arteriosclerotic atrophy by Cordes.[90] Diathermy has seemed to be

88. Abadie: De l'atrophie tabetique des nerfs optiques et de son traitement, Ann. d'ocul. **160**:385, 1923.

89. Springovitsch, G.: Ueber die Ergebnisse der Behandlung von Sehnervenatrophie mit retrobulbären Atropininjektionen, Klin. Monatsbl. f. Augenh. **90**:343, 1933.

90. Cordes, F. C.: Retrobulbar Injections of Atropine in Arteriosclerotic Atrophy, Am. J. Ophth. **20**:53, 1937.

beneficial in some cases in my experience but I have not tried atropine. The use of vasodilating drugs (nitrites, acetylcholine) seems to have had little permanent effect.

In discussing senile amblyopia, de Schweinitz [91] referred to Uhthoff's description of acute neuritis due to cerebral arteriosclerosis. The neuritis is rapid in onset and prompt in subsidence, with resulting atrophy of the optic nerve and shrinking of the retinal vessels.

According to Rones [8] colloid bodies are frequently found in the optic nerve and sheath of elderly persons when no atrophy of the nerve is present (fig. 13), and in the cases I have observed the vision has been undisturbed. These colloid bodies exhibit the staining reactions of amyloid and seem to develop from the neuroglial tissue.

OCULAR TUMORS

Retinal glioma with small cells in a sexagenerian has been described.[92]

Melanotic tumors of the choroid are usually seen in later life. In 1,416 cases of malignant intraocular melanoma studied by Callender, Wilder and Ash [93] the average age was 53 years and 833 of the patients were between the ages of 50 and 79.

In the classification of malignant melanoma of the choroid by histologic type, Wilder and Callender [94] found that the epithelioid cell type appears to be the most malignant and spindle cell subtype A relatively benign. The mixed type is second in malignancy to the purely epithelioid tumor. In the classification by fiber content, the malignancy of the tumor appears to be inversely proportional to the degree of intercellular invasion by argyrophil fibers. No deaths have occurred from any spindle cell subtype A or fiber content type 3 tumor, but all the patients in whom no argyrophil fibers appeared among the tumor cells have died (fig. 14).

GLAUCOMA

Glaucoma is predominantly a disease of the aged. The census in 1920 stated that in nearly one-half the cases it occurred between the ages of 45 and 64. According to this census, in 1920 it was nine times as prevalent as in 1890 and about one and a half times as prevalent as in 1910. The employment of the tonometer may be the most important cause of the apparent increase in the incidence of glaucoma.

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91. de Schweinitz, G. E.: Senile Changes in the Optic Nerves: So-Called Senile Amblyopia, Am. J. Ophth. **8**:400, 1925.

92. Sempé; DéJean, C., and Harant, H.: Gliome de la rétine à petites cellules chez un sexagénaire, Arch. Soc. d. sc. méd. et biol. de Montpellier **13**:554, 1932.

93. Callender, G. R.; Wilder, H. C., and Ash, J. E.: Personal communication to the author.

94. Wilder, H. G., and Callender, G. R.: Malignant Melanoma of the Choroid. Am. J. Ophth. **22**:851, 1939.

Senile changes which may contribute to the development of glaucoma include an increase in thickness and a loss of distensibility of the sclera, vascular changes, normal growth and swelling of the lens in beginning cataract and lessened size of the anterior chamber, which

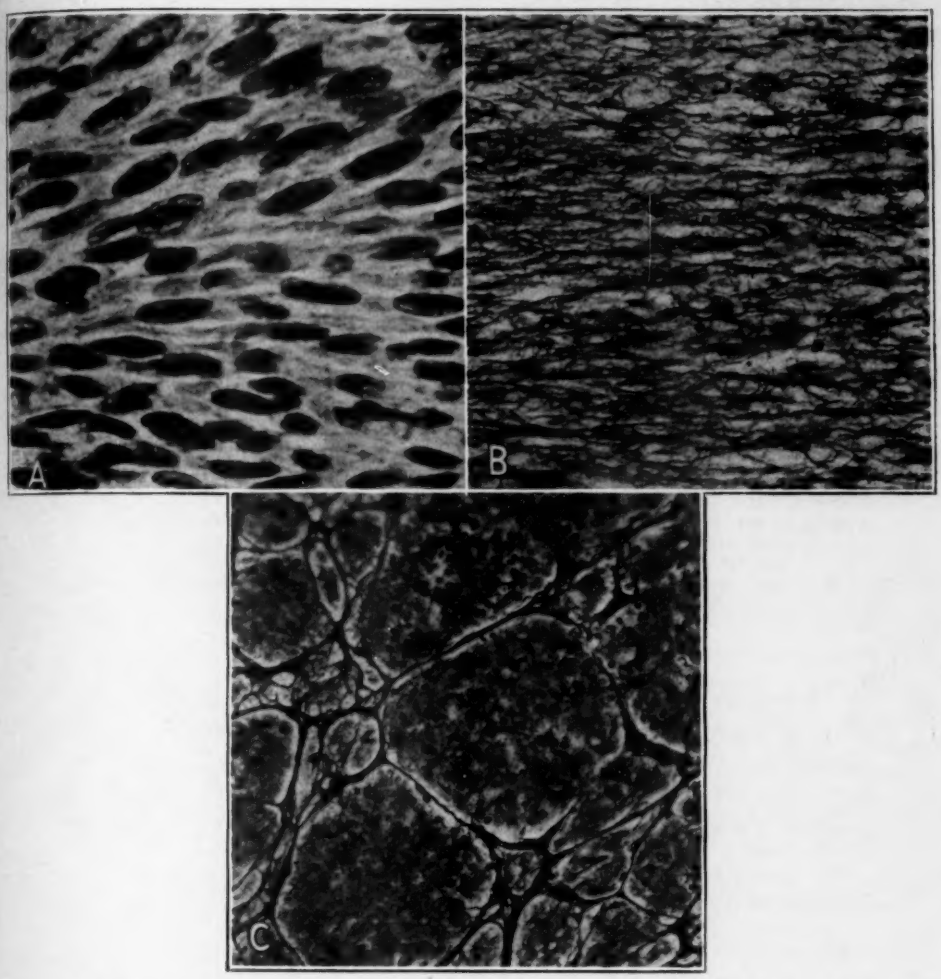

Fig. 14.—Types of malignant melanoma of the choroid (United States Army Medical Museum). *A*, spindle cell subtype *A* (× 1,000); *B*, fiber content type 3 (× 705); *C*, fiber content type 1 (× 330).

causes a decrease in the filtration angle and a pressing together of the meshes of the ligamentum pectinatum. Sclerosis of the ciliary processes and their encroachment on the circumlental space may also be a factor.

Reduction in the filtration angle should be avoided in the aged because, as Gradle [95] has shown, tension after the use of a mydriatic increases in direct proportion with age. He found that the curve of pressure according to age is fairly uniform, being lowest in the 30 to 40 decade, rising steadily to a maximum in the 60 to 70 decade and decreasing after the age of 70 (table 2). However, even in primary glaucoma, provided it is of the "wide angle" type, mydriatics are not contraindicated, as Koellner and Kronfeld have shown that dilating the pupil in patients with this type of glaucoma does not dangerously increase tension.

Moreover, the aqueous probably changes with age. Krause [96] has stated: "I have good reason to believe that the amount of lactic acid decreases and perhaps the dextrose in the aqueous increases with age." Glaucoma should be differentiated from optic nerve atrophy with cupping associated with sclerosis of the cerebral arteries, so that unnecessary operations may be avoided.[97]

TABLE 2.—*Effect of Mydriatics on Intraocular Tension (from Gradle* [95])

	Age						
	30-40	40-50	50-60	60-70	70-80	80+	Average
Number of eyes	300	236	176	196	74	18	.....
Average pressure in mm. of mercury	18.91	19.20	20.05	20.18	18.93	19.30	19.63
Eyes in which pressure increased more than 4 mm. of mercury after use of a mydriatic, percentage	2.9	2.1	2.2	2.0	5.3	11.1	4.26

PREVENTION OF THE AGING PROCESS

Hereditary factors [98] seem to be exceedingly important in the development of certain ocular and other physical signs attributable to age. Hereditary ocular lesions can be prevented only through eugenics, but some population trends seem to work naturally for prevention. For example, the growth of cities in Europe is credited [99] with the improve-

95. Gradle, H. S.: The Effects of Mydriatics upon Intraocular Tension, Am. J. Ophth. **19**:37, 1936.

96. Krause, A. C.: Personal communication to the author.

97. Knapp, A.: On the Association of Sclerosis of the Cerebral Basal Vessels with Optic Atrophy Cupping: Report of Ten Cases, Tr. Am. Ophth. Soc. **30**:343, 1932.

98. Vogt, A.: Weitere Augenstudien an eineiigen Zwillingen höheren Alters über die Vererbung der Altersmerkmale, Klin. Monatsbl. f. Augenh. **100**:497, 1938. Vogt, A.: Die senile Determination des Keimplasmas, beobachtet an eineiigen Zwillingen des 55-81. Jahres, Schweiz. med. Wchnschr. **65**:576, 1935. Crisp, W. H.: Hereditary Ocular Disorders of Senescence, Am. J. Ophth. **21**:1172, 1938.

99. Haldane, J. B. S.: New Paths in Genetics, New York, Harper & Brothers, 1942; Statistical Methods Aid in Human Heredity Study, Science News Letter **41**: 195, 1942.

ment of human heredity through the wiping out of hereditary defects. When people lived and died in the same village circle, cousins marrying cousins for generation after generation, defects resulting from recessive genes kept cropping up as a result of this inbreeding. But when people began to migrate and to mix the population, human outbreeding became the rule, and many of the once common defective genes eventually became lost.

Certain mental and physical changes which may develop with age seem to be benefited by the following of certain rules. Stoddard [100] proposed three rules to be used in fighting off oncoming mental old age: (1) avoid bad health conditions, (2) avoid the mechanisms of escape from life and reality—retrospection and rigidity—and (3) avoid lack of mental exercises. The same rules seem to be effective to a certain extent in preventing the physical deterioration often attributed to age. Certainly athletes who have kept up exercises regularly are usually more resistant to fatigue than those who stop physical activity because they are growing older.

Avoidance of overfatigue,[101] with the resulting toxic disturbances, may be one important factor in postponing the development of senile disturbances. Avoidance of tobacco and alcohol, especially by persons who have unpleasant symptoms from small amounts and by persons with chronic sinus disease, is also important if senility is to be deferred. Naturally, good hygenic living, with plenty of fresh air, sunshine and exercise [102] suited to individual needs, is beneficial.

I cannot help but believe that chronic infections, even those which are symptomless (quiet sinusitis and alveolar abscesses), play a part in the aging process, and these should be prevented, combated and if possible eliminated. Certainly nothing can make one feel older or act older than several alveolar abscesses or a small undrained focus in the nasal accessory sinuses. My personal and research experience leads me to believe that some of the circulatory and pathologic so-called ocular changes are caused by endotoxins.[103] More intelligent treatment of

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100. Stoddard, G. D.: Patterns of Growth in Human Intelligence, Proc. Nat. Acad. Sc. **27**:551, 1941.

101. Laird, D. A.: Fatigue, in Piersol, G. M.: Cyclopedia of Medicine, Philadelphia, F. A. Davis Company, 1939, vol. 6, p. 246.

102. Crampton, C. W.: Start Today! Your Guide to Physical Fitness, New York, A. S. Barnes & Company, 1941.

103. Berens, C.; Connolly, P. T., and Chapman, G. H.: Focal Infection in Diseases of the Eye: I. Report of Certain Laboratory Examinations, Brit. J. Ophth. **18**:463, 1934. Chapman, G. H.; Berens, C.; Lieb, C. W.; Rawls, W. B., and Stiles, M. H.: Examination of Cultures from Persons Suspected of Having Chronic Infection, Am. J. Clin. Path. **9**:491, 1939. Berens and Nilson.[27b] Berens and others.[27c]

constitutional factors should aid in preventing deterioration. According to Aschner [104] one should treat not only single organs or diseases but the entire personality. Dark-complexioned persons seem to have a higher percentage of gallstones, renal calculi, gout, diabetes and cancer. Blonds frequently require tonic and antilymphatic remedies, while brunets usually require eliminative treatment. In middle age the body often changes from the slender to the stocky type, with resulting changes in metabolism, endocrine balance and morbid disposition. By using foresight in constitutional therapy, one may be able to avert harmful excesses and pathologic changes in many organs.

In the abiotrophies one should not only know and recognize the ocular signs of death but try to save the tissues as long as possible by removing exogenous toxins, such as tobacco and alcohol, and endogenous toxins (especially from chronic and other foci of infection); by increasing the circulation (general and local), and by assuring an adequate supply of nutrient material through the blood stream.

SUMMARY AND CONCLUSIONS

Because the life expectancy of the average person has increased, it is evident that ophthalmologists will be concerned increasingly with the treatment of the eyes of the aged.

There seems to be little question that faulty circulation and degeneration, the result of vascular changes, are responsible for many of the serious visual disturbances of adults often attributed to age. What the physiologic and clinical changes in the blood serum are which increasingly inhibit cell growth is unknown, but when they are understood it may be possible to gage physiologic age. Although the role of abiotrophies should not be underestimated and it is difficult if not impossible to evaluate the role of chronic infection in the aging process, I am forced to the conclusion, mainly on clinical grounds, that many of the so-called old age processes in the eyes are caused directly or indirectly by infection.

In the orbit the most prominent sign of senility is the hollow-eyed appearance.

The conjunctiva, although it thickens near the cornea, becomes less elastic, which makes it more difficult to manipulate in operations.

Tenon's capsule becomes thicker, less elastic and infiltrated with fatty masses.

The increasing weakness of convergence observed in elderly persons is probably the result of diminished circulation from arteriosclerosis and possibly from absorption of endotoxins.

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104. Aschner, B.: Constitutional Therapy as a New Trend of Medicine, New York Physician **18**:32, 1942.

The sclera thickens, becoming more rigid and yellow with age. The inner canals, the canal of Schlemm and the external canals widen in old age (Theobald).

Corneal astigmatism and lenticular astigmatism increase slightly with age, although the total refraction of the cornea diminishes. After the age of 50 the corneal sensitivity decreases rapidly.

The anterior and the posterior chamber tend to become more shallow with age. The pigment found in the angle of the anterior chamber has been considered a senile change. However, because of the frequently observed evidence of quiet iritis in many old persons, the condition may be a mild inflammatory change.

The function of the ciliary muscle probably lessens to some extent, as a result of sclerosis of the vessels and fibrosis.

The delicate capillary network of the choroid becomes irregular in old persons, and many variations in caliber are noted. Varying degrees of degeneration are observed in the larger vessels, and the choroidal vascular changes probably underlie many of the retinal lesions. Decreased circulation affects the pigmented epithelium. Drusen, which are often considered as senile changes, may be the result of a mild toxic disturbance.

Although the treatment of senile degeneration of the macula (senile macular chorioretinitis) is usually considered useless, at times the recurrence of small hemorrhages seems to have been prevented by eliminating chronic infections and increasing resistance against them. Indulgences (use of alcohol and tobacco) which apparently have little deleterious effect on young ocular tissues and functions, in the aged may cause functional impairment or serious organic change.

The weight of the lens increases with age. The gradual dehydration and sclerosis of the cortical lens fibers cause the lens to become practically all nucleus in advanced age. These changes cause an increase in the index of refraction of the outer layers, diminish the convexity of the lens surfaces, lessen plasticity and apparently account in large part for the inertia of adjustment of the eye to clear seeing at different distances and for the development of presbyopia.

Biomicroscopy often reveals colloid deposits on the anterior lens capsule, an increase in the internal diffuse reflection of light and an increase in the visibility of the surface of the adult (senile) nucleus.

Although cataract is commonly observed in old age, it is questionable whether age is an important factor, and age per se is no contraindication to operation. Cataract secondary to uveitis may affect one eye, and focal infection apparently may also play an important role, even though the eye may show no evidence of inflammation. Although there is no

method of absorbing lens opacities and visual acuity is an unreliable criterion of the effect of treatment, improved general health and local circulation seem to retard the progress of some cataracts which apparently are not demonstrably secondary.

After the age of 60 there is a tendency toward lower hyperopia and actual, progressive myopia. This so-called second sight may be the forerunner of lowered visual acuity and cataracts. There is a slight increase in corneal and lenticular astigmatism after 50.

Age may be the most important factor in the adaptation of the intensity of light for clear seeing, and the adjusting of intensity to meet the requirement of age is exceedingly important, if not the major problem, in the grading of intensity in lighting practice.

The retinal changes in diabetes seem to bear a definite relation to age, as the average age for the appearance of diabetic retinopathy is 55 years, but the exact cause of the retinal hemorrhages is a baffling problem, and their treatment is unsatisfactory.

Partial senile atrophy of the optic nerve has been observed in the aged, and senile optic neuritis has been reported. The former is probably caused by partial or complete closure of the arterioles in the nerve and the latter by cerebral arteriosclerosis.

Malignant tumors of the choroid are usually seen in later life, the average age for their discovery being 53 years. The malignancy of the tumors appears to be inversely proportional to the degree of intercellular invasion by argyrophil fibers.

Senile changes, such as fragments of capsule, quiet iritis with pigmentary disturbance, sclerosis of the pectinate ligament, shallowing of the anterior chamber and alterations of the chemistry of the aqueous probably contribute to the development of glaucoma, which is predominantly a disease of the aged. Postmydriatic tension increases with age, reaching a maximum between 60 and 70 years. Therefore, miotics should be used to contract pupils which have been dilated in older patients.

Although one can prevent hereditary conditions only through eugenics, the abiotrophies should be recognized, and, even though treatment is unsatisfactory, endogenous and exogenous toxins should be eliminated and circulation and nutrition improved. Certain mental and physical changes which may develop with age seem to be benefited by the following of certain rules. Overfatigue, with the resulting toxic disturbances, may be an important factor in the development of functional and even pathologic senile changes. Good hygienic living, with adequate rest and sleep, a well balanced diet containing sufficient vitamins and plenty of fresh air, sunshine and exercise suited to individual needs, probably is beneficial in delaying general and ocular manifestations of age.

Chronic infections seems to play a part in the aging process of the eye and in its diseases; therefore infections should be prevented from developing or becoming chronic, combated if they do gain a foothold and if possible completely eliminated.

If biochemical studies of blood serum finally disclose the secret of prolonging life, it will be even more important for ophthalmologists to control hereditary, nutritional, toxic and other factors which predispose to or cause diseases seen in old eyes.

35 East Seventieth Street.

DEVELOPMENTAL CATARACTS

RESULTS OF SURGICAL TREATMENT IN ONE HUNDRED AND THIRTY-ONE CASES

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Analyses of surgical results have an excuse for being, since they substantiate or refute commonly accepted practices and frequently indicate the need for a more satisfactory approach to a given problem.

This paper summarizes the results of surgical treatment in 131 cases of developmental cataracts at the ophthalmic clinic of University Hospital between the years 1925 and 1942. No case was included in this series unless the history indicated that the cataract was noted at birth or shortly thereafter by the parents or by the referring physician. For the most part, the surgical procedure utilized was discission, repeated as frequently as necessary to obtain a clear pupillary opening. Linear extraction was employed whenever indicated, that is (*a*) when the anterior chamber was filled with fluffy degenerating cortical material, (*b*) when there was secondary glaucoma, the result of a too rapidly swelling lens, or (*c*) when it was desirable to hasten the clearing of the pupillary area because, for obvious reasons, the postoperative management of the patient was to be jeopardized by inexperienced physicians or the parents could not be trusted. Linear, intracapsular and extracapsular extraction were employed whenever the age of the patient or the ocular conditions warranted.

Developmental cataracts, exclusive of complicated, coronal and subcapsular opacities of an endocrine or metabolic origin, are an interesting study. To a large extent ophthalmologists are ignorant of their primal causes, especially in regard to the mechanism of their production and the rationale of their transmission from one person to another. Perversions of lenticular development result from either (1) an inherent defect in the germ plasm or (2) a noxious external agent acting on a normal germ plasm. Except for scattered genealogic tables of questionable informative value, knowledge concerning the first factor is

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indeed scant.[1] Recent investigations into the physicochemical, pathologic, metabolic and endocrine aspects of the development of cataracts have contributed greatly to the understanding of the influence of noxae on normal germ plasm.[2] Mann [3] and von Szily [2] have both reported actual idiokinetic disturbance resulting in malformation of the lenticular anlage.

A classification of developmental cataracts is not within the scope of this presentation.[4] The correct diagnosis is essential and largely determines the need for surgical intervention. A thorough knowledge of the structure of the lens, particularly the zones of discontinuity,[4a] revealed under the slit lamp is prerequisite to correct diagnosis. With such knowledge the physician is able to place rather accurately the time at which the pathologic aberration of structure occurred in the development of the lens.

The ophthalmologist accepts a great responsibility in treating a developmental cataract, since by his success or failure the patient's future position in society is largely determined. Such patients are compelled to compete for a livelihood in an era in which high and precise ocular requirements are emphasized. Lowered visual acuity, effected by the cataract, as well as associated neural receptor defects probably present, severely handicap them in securing an education as well as a vocational occupation in competition with normal persons. Successful surgical treatment is unfortunately the best there is to offer, and, even though excellent visual acuity is frequently obtained, the ever present heavy and disfiguring spherical lenses are in themselves a great handicap. The physical development is greatly curtailed both by the glasses and by the frequently associated lack of satisfactory binocular vision. The psychic trauma to the growing child is equally great. Personality changes are effected by the realization that one is "afflicted and different" and frequently physically as well as mentally inferior to one's associates. The fact that the affected persons possess poor protoplasm will be reemphasized later.

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1. Mann, I. C.: The Development of the Human Eye, London, Cambridge University Press, 1928, p. 66.

2. von Szily, A.: Doyne Memorial Lecture: Contribution of Pathological Examinations to the Elucidation of Problems of Cataract, Tr. Ophth. Soc. U. Kingdom **58**:595-660, 1938.

3. Mann, I. C.: Developmental Abnormalities of the Eye, London, Cambridge University Press, 1937, p. 316.

4. (*a*) Koby, F. E.: Slit-Lamp Microscopy of the Living Eye, translated by C. Goulden and C. L. Harris, Philadelphia, P. Blakiston's Son & Co., 1930, p. 219. (*b*) Duke-Elder, W. S.: Textbook of Ophthalmology, St. Louis, C. V. Mosby Company, 1938, vol. 2, p. 1358. (*c*) Mann.[3]

The surgical procedures utilized in the treatment of developmental cataracts are rather limited. They include visual iridectomy, discission, combined discission and linear extraction, linear extraction and intracapsular or extracapsular extraction. Cycles of popularity have been enjoyed by the majority.

The ophthalmic literature contains the writings of not a few advocates of visual iridectomy as the treatment of choice, especially in the case of incomplete lenticular opacities. Some suggest that a 3 mm. coloboma be placed down and in, to increase reading comfort and to aid in the obtaining and preserving of binocular vision.[5] Others emphasize the placing of a coloboma superiorly, with the thought in mind of possible surgical intervention later in life.[6] In the limited experience with visual iridectomy at the ophthalmic clinic of University Hospital, the procedure has not proved to be a satisfactory approach.

Discission has many advocates because of safety, simplicity of technic and a fairly good ratio of satisfactory visual results.[7] Clapp [8] and Goldsmith have carefully worked out the fact that the lens substance is readily absorbed when traumatized and exposed to the aqueous by discission of the capsule. The postulated enzymic protogenous splitting faculty of the aqueous is now fairly well accepted. Wilder,[7a] Greenwood,[7b] McReynolds,[7c] Spaeth [9] and a host of practitioners are advocates of this method of surgical intervention. Ziegler,[10] who has modified simple discission to a through and through V-shaped incision of the lens, has many followers. Such widely recognized ophthalmic surgeons as Benedict,[11] Wiener and Alvis [12] and Berens,[13] as well as many other surgeons, have said that they use the technic and have highly recom-

5. Fox, L. W.: Congenital Cataracts, J. A. M. A. **89**:2249-2252 (Dec. 31) 1927.

6. Bell, G. H.: Operation for Juvenile Cataract in Two Stages, Am. J. Ophth. **9**:433-435 (June) 1926.

7. (*a*) Wilder, W. H.: The Operative Procedures and Method of Handling Juvenile Cataract, Tr. Am. Acad. Ophth. **33**:113-131, 1928. (*b*) Greenwood, A., in discussion on Wilder. (*c*) McReynolds, J. O.: Congenital Cataracts, Texas State J. Med. **25**:612-615 (Jan.) 1930.

8. Clapp, C. A.: Cataract: Its Etiology and Treatment, Philadelphia, Lea & Febiger, 1934, p. 96.

9. Spaeth, E. B.: The Principles and Practice of Ophthalmic Surgery, Philadelphia, Lea & Febiger, 1939, p. 530.

10. Ziegler, S. L.: Complete V-Shaped Discission for Zonular and Pyramidal Cataracts, Am. J. Ophth. **5**:381 (May) 1922.

11. Benedict, W. L., in discussion on Dean, F. W.: Cataracts: Operation for Congenital and Juvenile, Tr. Am. Acad. Ophth. **31**:261-270, 1926.

12. Wiener, M., and Alvis, B. Y.: Surgery of the Eye, Philadelphia, W. B. Saunders Company, 1939, p. 54.

13. Berens, C., in discussion on Dean, F. W.: Cataracts: Operation for Congenital and Juvenile, Tr. Am. Acad. Ophth. **31**:261-270, 1926.

mended it. Some have modified Ziegler's procedure in slight detail. For instance, Bell [6] described an initial iridectomy followed in four weeks by the Ziegler discission. He expressed the opinion that capsular incision is thereby greatly facilitated. The chief points of objection are (1) delayed absorption, (2) presence of vitreous if the anterior chamber needs to be opened later and (3) traumatizing of the vitreous body, which is frowned on by many surgeons. It is interesting to note in passing that Ballantyne [14] reported performing discission by attacking the posterior capsule by way of the pars planum, pleading slower absorption and less frequent secondary glaucoma and iridocyclitis.

A combination discission and linear extraction is popular. The accepted surgical technic most widely employed is first to perform a discission of the anterior lens capsule combined with moderate stirring of the cortical parenchyma. Postoperatively the patient is observed closely for several days until the proteolytic action of the aqueous has effected sufficient disintegration of the lens cortex to permit evacuation through a corneal or limbal keratome incision. The position of the keratome incision varies with individual surgeons, being in a limbal, subconjunctival limbal or corneal site. Corneal incisions are felt to be less frequently complicated by prolapse of the iris. Horay [15] summarized the results of various operative procedures in 151 cases and reported the best results when a combination of discission and linear extraction was utilized. Other procedures, such as suction extraction of soft cortical material, are merely modifications of this method.

Simple linear extraction performed at one setting, while not original with him, was revived by Barkan [16] in 1932. He advocated a corneal incision and anterior capsulectomy followed by thorough irrigation or massage of the cortical and nuclear material from the pupillary area. His innovation is an oblique corneal incision which serves as a valve flap assuring the rapid reformation of the anterior chamber. Prolapse of the iris is relatively infrequent, a clear pupillary opening is secured nearly at once and the postoperative reaction is minimal. Favorable comment of late has been accorded this procedure, and the technic is being widely utilized in the treatment of many types of cataracts. According to the experience of the ophthalmic clinic it is best applied to the treatment of soft cataracts.

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14. Ballantyne, A. J.: A Case of Congenital Cataract with Unusual Features, Tr. Ophth. Soc. U. Kingdom **51**:103-107, 1931.

15. Horay, G.: Ueber Staroperationen im Kindesalter, Klin. Monatsbl. f. Augenh. **74**:178-184 (Jan.-Feb.) 1925.

16. Barkan, O.: A Procedure for the Extraction of Congenital, Soft, and Membranous Cataracts, Am. J. Ophth. **15**:117-124 (Feb.) 1932.

We have limited intracapsular cataract extraction to the treatment of shrunken, dense, membranous or hard cataracts in the very young. For added safety a Kuhnt conjunctival flap is always employed in conjunction with a sclerocorneal incision.

AGE AT OPERATION

A wide variance of opinion exists regarding the most suitable age for the patient to be when one operates on a congenital cataract. Fuchs [17] stated in his excellent textbook that a congenital cataract should be operated on early to prevent amblyopia and to insure both ocular and mental development. More modern disciples of this viewpoint are Wiener and Alvis,[12] Blaauw [18] and Horay.[15] Treacher Collins,[19] who without a doubt has been the greatest contributor to knowledge of congenital cataracts, expressed the opinion that it is best to wait until the child is at least 10 months old, at which time the anterior chamber will be deeper and larger. Wilder [7a] and Greenwood [7b] said they prefer to operate on one eye early in life if the child possesses complete cataracts and to wait until later if the cataracts are incomplete and the child can get around and play.

Several German ophthalmologists, including Kiss,[20] Grod and Kuhnt, have reported discouraging results when operation was performed during the first year of life. Elschnig, quoted by Fleischer,[21] advised early operation if there is complete cataract bilaterally. He suggested that if the cataract is incomplete and some vision can be obtained, surgical intervention be postponed until the eighth year of life. Seefelder and Fleischer stated that they wait until the third or fourth year of life before attempting operation. Louis Bothman said that he will operate as early as the age of 6 months but prefers waiting until the child is at least 1 year old.

ANALYSIS OF SURGICAL RESULTS

No patient was operated on if the preoperative visual acuity could be demonstrated to be better than 6/15 or its equivalent.

Of the 131 patients, 61.7 per cent were males and 38.3 per cent females (table 1).

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17. Fuchs, E.: Text-Book of Ophthalmology, translated by A. Duane, ed. 5, Philadelphia, J. B. Lippincott Company, 1917, p. 551.

18. Blaauw, E., in discussion on Wilder.[7a]

19. Collins, E. T.: Developmental Deformities of the Crystalline Lens, Ophthalmoscope **6**:577-583 and 663-676, 1908.

20. Kiss, W.: Sehschärfe der in früher Kindheit doppelseitig Staroperireten, Klin. Monatsbl. f. Augenh. **98**:523-531 (April) 1937.

21. Fleischer: Zeitpunkt für die Operation eines angeboren Stares, Klin. Monatsbl. f. Augenh. **103**:329 (Sept.) 1939.

When more than one developmental aberration was present in a single lens, only the predominating type was classified (table 2). The high percentage (38.1 per cent) of zonular cataracts was expected. It might be even higher if one were able to reexamine the cataracts previously classified as nuclear, particularly in view of the improvement in slit lamps and of modern conceptions of cataract pathology.

TABLE 1.—*Patients Grouped According to Sex*

	Number	Percentage
Male	81	61.73
Female	50	38.27
	131	100.00

TABLE 2.—*Types of Cataract*

	Number of Eyes	Percentage
Zonular	93	38.11
Nuclear	59	24.18
Soft	33	13.52
Punctate	16	6.55
Fusiform	14	5.74
Coralliform	8	3.27
Anterior polar	7	2.86
Posterior polar	5	2.045
Fibrous	4	1.64
Disciform	2	0.82
Anterior polar with impression	2	0.82
Posterior star	2	0.82
Total	245	100.00

TABLE 3.—*Hereditary or Familial Tendency*

	Number of Cases	Percentage	
Proved	22	16.0	
Questionable	2	1.53	Total cases, 131

Fusiform cataract, an axial aberration, is rare (Duke-Elder). It is indeed possible that with careful slit lamp examinations a few of those reported in the present series would be reclassified in view of recent literature.

The two disciform cataracts were typical, being doughnut shaped, with a small but distinct, clear equatorial cortical ring and a thin opaque membranous axial sheet. Reports of such cataracts, which possibly result from aplasia of the primary, or embryonic, nucleus, are rare in the literature.

Proved inheritance or a familial tendency was present in 16 per cent, or 22, of the cases (table 3). In 1.5 per cent, or 2, of the cases there was a questionable history of hereditary cataractous defects. Present investigation into the genealogic trees in many cases of this series is indicating that a far greater percentage is to be expected.

TABLE 4.—*Type and Number of Operations*

Type of Operation	Number	Percentage
Discission	413	81.0
Linear extraction	64	12.5
Extracapsular extraction	15	2.9
Intracapsular extraction	7	1.3
Extraction of secondary lens membrane	5	0.9
Iridocapsulotomy	4	0.3
Visual iridectomy	2	0.7
Number of eyes operated on, 233	510	99.7+
Surgical Treatment of Complications		
Accidental iridotomy	4	
Iridectomy for prolapsed iris	4	
Cyclodialysis	4	
Excision of anterior synechia	2	
Trephining	1	
Lagrange sclerectomy	1	
Paracentesis	1	
Enucleation	1	

TABLE 5.—*Final Visual Acuity* *

	Number of Eyes	Percentage	
I. Distant Visual Acuity			
6/ 4.5 — 6/ 7.5	36	15.4+	
6/ 9 — 6/12	47	20.1+	
6/15 — 6/30	42	18.0+	
6/60 — W. B.	21	9.0+	
5/60 — M. O.	24	10.2+	
L. P. — nil	15	6.4	
Not recorded	48	20.6	Total, 233
II. Near Visual Acuity			
J. 1 — J. 3	58	24.8	
J. 4 — J. 7	43	18.4	
J. 11 — J. 14	22	9.4	
No. J.	15	6.4	
Not recorded	95	40.3	

* In this and in the following tables, W. B. indicates ability to place Worth's ball; M. O., ability to distinguish moving objects; J., ability to read Jaeger's test type of the given number, and L. P., light perception.

Table 4 classifies the operations as to type, number and frequency. The 413 discissions constitute 81 per cent of the surgical procedures. A total of 233 eyes were operated on. Sixty of the 64 linear extractions were performed to relieve the anterior chamber of swelling cortical material. The greatest number of discissions performed on any one eye was 6.

The final visual acuity for distance is, on the whole, satisfactory, 53.5 per cent of 233 eyes having 6/30 or better vision (table 5). Nine per cent are capable of 6/60 vision or possess the ability to place accurately the 5 mm. Worth ball. For all practical purposes 16.8 per cent are blind or nearly so and must be considered as debits to society. The visual acuity of 20.6 per cent could not be recorded because of the age of the patient, lack of cooperation or mental deficiency.

Fine and discriminative visual acuity for reading is possessed by 24.8 per cent. Eighteen and four-tenths per cent are at least capable of reading Jaeger 4 to 7 type print. This is equivalent to the print utilized in the textbooks employed in the lower school grades.

TABLE 6.—*Age of Patients When Operated On*

Age, Years	Number of Patients	Percentage
0 — 0.9	16	12.20+
1 — 1.9	7	5.30
2 — 2.9	3	2.28
3 — 3.9	9	6.87
4 — 4.9	6	4.56
5 — 5.9	4	3.00
6 — 6.9	9	6.87
7 — 7.9	7	5.30
8 — 8.9	11	8.39
9 — 9.9	1	0.76
10 — 10.9	10	7.63
11 — 11.9	5	3.81
12 — 12.9	4	3.00
13 — 13.9	3	2.28
14 — 14.9	0	0.00
15 — 15.9	3	2.28
16 — 16.9	2	1.52
17 — 17.9	3	2.28
18 — 18.9	2	1.52
20 — 20.9	3	2.28
21 — 30	9	6.87
31 — 40	3	2.28
41 — 50	7	5.30
51 — 60	1	0.76
61 — 70	1	0.76

Average age, 11.15; patients, 131.

Grouping the patients according to age at the first operation disclosed, as anticipated, that 55 per cent were operated on under the age of 8 years (table 6). Seventeen and five-tenths per cent were operated on under the age of 2 years. The average age at operation for the entire series was 11.1 years. The youngest patient was 5 weeks old. The oldest patient was 67.

Twenty per cent of all failures (from light perception to no vision) occurred in the patients operated on during the first year of life (table 7). If the patients operated on in the first two years are totaled, one third, or 5, of all the failures occurred in the group. Of the unsatisfactory results (vision from 5/60 to perception of moving objects), 24

per cent occurred in this combined group and 20 per cent in the patients operated on under 1 year of age. In respect to final visual acuity, the best results were secured when the patient was first operated on between the ages of 4 and 10 years. One must consider, however, that the children operated on during the first year of life represent those with complete cataracts and thus offer a poorer prognosis. The majority

TABLE 7.—*Age at Operation in Relation to Final Visual Acuity*

Age, year	0-0.9	1-2	3-4	5-7	8-10	11-20	21-30	31-40	41-50	51-60	61-70
I. Distant Visual Acuity											
6/ 4.5 - 6/ 7.5	0	0	4	8	6	5	6	1	6	0	0
6/ 9 - 6/12	0	0	2	10	16	10	3	1	4	0	1
6/15 - 6/30	4	0	4	9	8	14	1	0	1	1	0
6/60 - W.B.	3	2	3	4	5	0	4	0	0	0	0
5/60 - M.O.	5	1	5	1	0	9	1	1	0	1	0
L. P. - nil	3	2	2	5	2	0	0	1	0	0	0
Not recorded	18	13	8	0	1	7	0	0	0	0	1
II. Near Visual Acuity											
J. 1 - J. 3.	2	0	3	14	11	10	8	2	8	0	0
J. 4 - J. 7	1	0	1	8	11	16	4	0	2	0	1
J. 11 - J. 14	2	0	7	6	4	3	0	0	0	0	0
No J.	3	0	1	2	3	1	1	2	1	1	0
Not recorded	25	18	16	7	9	15	2	0	0	1	1
No. of cases	18	10	14	20	20	28	9	3	7	1	1

TABLE 8.—*Final Visual Acuity in Relation to Type of Operation*

	Discission	Combined Discission and Linear Extraction	Simple Intracapsular or Extracapsular Extraction	Simple Linear Extraction
I. Distant Visual Acuity				
6/ 4.5 - 6/ 7.5	20	11	5	..
6/ 9 - 6/12	23	17	6	..
6/15 - 6/30	32	7	2	..
6/60 - W.B.	21	3	1	..
5/60 - M.O.	20	5	1	..
L. P. - nil	11	3	1	1
Not recorded	39	5	1	..
II. Near Visual Acuity				
J. 1 - J. 3	36	13	5	..
J. 4 - J. 7	22	18	5	..
J. 11 - J. 13	24	2	0	..
No J.	18	6	0	1
Not recorded	66	12	4	..

of the children who were permitted to wait until they reached school age had sufficient visual acuity to enable them to get about. One may assume that in such cases the macular area of the retina receives the necessary physiologic impetus to development. Amblyopia ex anopsia may explain the poor visual acuity obtained in the lower age groups. It must be admitted that this is not the entire explanation, since the literature contains many reports of good visual acuity secured when complete cataracts had been neglected until the child was 4 or 5 years of age. Failure of development of the macular area is frequently asso-

ciated with microphthalmos; moreover, this anomaly is commonly seen with developmental cataracts. Poor visual acuity following successful surgical intervention may be explained by the failure of anatomic development of the macular area or of any portion of the visual pathway.

Of the eyes, 71.24 per cent were treated by discission and 21.8 per cent by discission combined with linear extraction (table 8). Of the patients treated by discission, 27.1 per cent achieved 6/12 or better

TABLE 9.—*Classification of Surgical Complications*

Surgical Complications	Number of Eyes	Comment
Secondary glaucoma	19	In 9 eyes this persisted after linear extraction
Secondary membranous cataract	19	69 eyes of 233 operated on experienced complications (29.6%)
Anterior synechia	11	
Postoperative iridocyclitis	11	
Loss of vitreous	9	
Incarceration of iris	6	
Iridotomy	4	
Glaucomatous optic nerve atrophy	5	
Retinal detachment	3	
Phthisis bulbi	3	
Hyphemia, severe	3	
Prolapsed iris	4	
Subluxation of lens	2	
Inclusion cyst of anterior chamber	1	
Subhyaloid hemorrhage	1	
Filtrating cicatrix	1	

TABLE 10.—*Final Visual Acuity in Eyes Showing Surgical Complications*

	Number of Eyes	Percentage
I. Distant Visual Acuity		
6/ 4.5 - 6/ 7.5	7	10.8
6/ 9 - 6/12	8	11.5
6/15 - 6/30	10	14.3
6/60 - W. B.	6	8.6
5/60 - M. O.	19	27.2
L. P. - nil	9	12.9
Not recorded	10	14.3
II. Near Visual Acuity		
J. 1 - J. 3	11	15.87
J. 4 - J. 7	12	17.3
J. 11 - J. 14	4	5.7
No J.	18	25.8
Not recorded	24	34.3
Total	69	100.0

Number of eyes operated on, 233; eyes showing surgical complications, 69; percentage, 29.6.

vision. Of those treated by discission and linear extraction combined, 54.9 per cent secured better than 6/12 visual acuity. Horay's experience was similar in that the combined procedure gave the best results in his series. Of the eyes treated by discission, 27.7 per cent, and of the eyes treated by the combined method, 25.4 per cent, were able to read Jaeger 1 to 3 test type for near vision.

Surgical complications of major or minor significance occurred in 69 of 233 eyes, or in 29.6 per cent (table 9). Of these complications, 28.9 per cent developed in eyes operated on by linear extraction. Secondary glaucoma developed in 19 eyes; in 10 of these linear extraction gave relief, but 9 eyes required further surgical intervention. This secondary glaucoma was difficult to control either medically or surgically, and glaucomatous optic nerve atrophy developed in 5 of the 9 eyes.

Of the eyes showing complications from surgical intervention, 22.3 per cent possessed a final visual acuity of better than 6/12 (table 10). The vision of 28 eyes, or 40 per cent, must be considered as lost (from 5/60 to no vision).

TABLE 11.—*Complications in Patients Operated on Under 2 Years of Age*

Complications	Under One Year (18 Patients)	Two Years and Under (10 Patients)
Secondary glaucoma	4	1
Subluxation of lens	1	3
Dense secondary membrane	2	4
Postoperative iritis	2	1
Anterior synechia	2	1
Incarceration of iris	1	1
Uveal prolapse	1	0
Phthisis bulbi	0	1
Associated Pathologic Condition		
Nystagmus	10	4
Microphthalmos	7	0
Congenital aniridia	2	0
Brain defect	3	1
Hypospadias	1	0
Strabismus	0	2
Congenital heart disease	0	1
Rickets	1	0
Hyperchromic metabolic anemia	1	0
Harelip	0	1

Of the surgical complications, those in 13 eyes, or 18.8 per cent of all surgical complications, were encountered in patients operated on before the age of 1 year (table 11). Of such complications, 17.4 per cent were encountered in patients operated on between the ages of 1 and 2 years. A total of 36.2 per cent, or more than one third of all the surgical complications, therefore, occurred in the patients operated on under 2 years of age. Thirty-three eyes were treated before the patient was 1 year of age.

Of the 131 patients in the series, 68, or 52.6 per cent, had some form of associated ocular disturbance (table 12). The frequency of associated nystagmus, strabismus, microphthalmos and subluxation of the lens emphasizes the poor protoplasm with which one deals in cases of developmental cataracts.

No patient with typical pendular or so-called ocular nystagmus achieved better than 6/15 visual acuity (table 13). The 6 patients securing better than 6/12 vision all had a vertical or rotatory type of nystagmus and a fast and slow component revealing that the nystagmus was of central origin.

TABLE 12.—*Associated Ocular Disturbance*

	Number	Comment
Nystagmus	41	Cases
Strabismus	34	Cases
Divergent	17	Alternating, 4; monocular, 13
Convergent	17	Alternating, 5; monocular, 12
Chorioretinitis	10	Cases
Central	17	Eyes
Peripheral	13	Eyes
Microphthalmos	12	Eyes
Subluxation of lens	6	Eyes
Congenital defect of iris	9	Eyes
Dissociated ocular movements	4	Cases
Eccentric fixation	6	Eyes
Coloboma of optic nerve	4	Eyes
Coloboma of lens	3	Eyes
Muscle paresis	3	Cases
Coloboma of choroid	2	Eyes
Hyaloid artery	1	Eye

Sixty-eight patients (52.6+%) displayed ocular disturbance

TABLE 13.—*Final Visual Acuity in Patients with Nystagmus*

	Number of Eyes	Percentage	Comment
I. Distant Visual Acuity			
6/ 4.5 - 6/ 7.5	1	1.32	All 6 eyes with better than 6/12 vision had a vertical or rotatory component
6/ 9 - 6/12	5	6.58	
6/15 - 6/30	17	22.36	
6/60 - W. B.	16	21.05	
5/60 - M. O.	11	14.47	
L. P. - nil	8	10.48	Only 2 eyes had a rotatory component.
Not recorded	18	23.68	
II. Near Visual Acuity			
J. 1 - J. 3	7	9.21	
J. 4 - J. 7	14	18.42	
J. 11 - J. 14	14	18.42	
No J.	12	15.79	
Not recorded	29	38.16	
Total eyes	76	(38 cases)	

Thirty-nine patients, or 29.7 per cent of the total, revealed associated disturbance of a constitutional variety, either congenital or metabolic (table 14). The high proportion of mental deficiency is noteworthy. Many authorities are of the opinion that the retarded mentality is due to failure to receive visual sensations. Numerous case reports have cited a pronounced improvement in the intellectual status after successful

operation for the cataract. Actual cerebral developmental dyscrasia is frequently present, and the ophthalmologist should be cautious in prognosticating normal mental development after a successful operation. Four of the patients with mental deficiency in this series have had to be institutionalized.

TABLE 14.—*Associated Specific and Constitutional Disturbance*

Pathology	Number of Patients	Comment
Mental retardation	17	Moron, 2; idiot, 1; imbecile, 1
Convulsive disorder	7	Entire life
Rickets	5	
Congenital heart lesion	4	
Malnutrition	3	
Oxcephaly	2	
Hyperchromic metabolic anemia	2	
Diabetes	2	
Umbilical hernia	2	
Clubfoot	2	
Harelip	2	
Congenital deafness	2	
Hypospadias	2	
Spastic paraplegia	2	
Congenital anomaly of esophagus	1	
Friedreich's ataxia	1	
Spina bifida	1	
Achrondoplasia	1	
Infantile genitalia	1	
Behavior problem	2	
Eccentric personality	1	
Pott's disease	1	
Hypoplasia of teeth	1	
Prematurity	1	
Obsessional neurosis	1	
Narcolepsy	1	

Number of patients showing these disturbances, 39, or 29.7 per cent of total.

TABLE 15.—*Microphthalmos*

	Final Visual Acuity	Number of Eyes
3/60 =	6/60	6
	M. O.	2
	L. P. — nil	2
Not recorded		4
Cases		7

Of 7 patients with microphthalmos, none secured better than 6/60 visual acuity in either eye (table 15). The presence of this condition indicates a poor prognosis for resultant good visual acuity.

CONCLUSIONS AND RECOMMENDATIONS

1. Persons with developmental cataracts are extremely likely to have associated ocular or constitutional congenital anomalies. These persons have poor protoplasm.

2. It is suggested that in the case of complete bilateral cataracts, operation be performed on one eye after the patient reaches 6 months of age. The other eye may be surgically treated after the age of 2.

3. If the cataracts are incomplete and the child can get around, surgical intervention should be postponed until the third or fourth year of life.

4. In the present series, in very young children discission of the lens capsule proved to be the safest technic, and although complications were frequent they were fortunately minor.

5. The best visual acuity was obtained when the combined technic of discission and linear extraction was employed.

6. Of 233 eyes, 83, or 35.5 per cent, obtained a final visual acuity of 6/12 or better and have permitted the patients to maintain a useful place in society.

7. Contraception is urged when the cataract is familial.

8. Sterilization is recommended when the offspring displays a lenticular defect which is proved hereditary.

9. Surgical intervention in early life is hazardous, as shown by the fact that a high percentage of complications and 33 per cent of the total failures (from light perception to no vision) occurred in the age group under 2 years.

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CONTACT ROENTGEN THERAPY OF SUPERFICIAL MALIGNANT LESIONS ABOUT THE EYE

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Radiologists frequently find malignant lesions in and about the eye difficult to treat. The protection of the lens and retinal structures presents a constant therapeutic problem. Even with the numerous protective devices which have been developed, it is frequently impossible to shield completely these structures from deleterious effects of roentgen rays and of radium radiation. In addition, the uneven facial contour about the eyes makes such lesions inaccessible and application of the usual types of apparatus difficult. Surgical treatment requires a delicate plastic procedure, which is usually kept to a minimum when more extensive surgical intervention is indicated.

The development of shock-proof "contact therapy" units, both of the water and of the air-cooled type, has helped solve many of the radiologic problems associated with such lesions. These units incorporate a small mobile shock-proof tube of low voltage, short target-skin distance and minimal filtration, the rays of which emerge axially from one end of the tube.

The distribution of doses approximates qualitatively that obtained with surface or interstitial use of radium, but the rate of delivery of energy is much higher. For instance, superficial basal cell carcinoma may be eradicated in less than sixty seconds.[1] The method constitutes a technic of cauterizing superficial lesions with roentgen rays, since most of the roentgen energy is absorbed in the top few millimeters of tissue. Likewise, the underlying structures are preserved, owing to the shallow penetrability of the radiation. The small size of the tube, the sharp dosage gradient in the tissues and the speed with which a large dose may be administered all give the method a special adaptability to the treatment of the lesions about the eye. Close cooperation with the ophthalmologist has made for good selection and care of patients with such lesions in the Brooklyn Cancer Institute.

1. Howes, W. E., and Camiel, M. R.: Contact Roentgen Therapy, Am. J. Roentgenol. **48**:360 (Sept.) 1942.

At this hospital an air-cooled type of unit is used. The tube is fitted into a compact shock-proof metal cylinder, and the rays emerge from one end like the light from a flashlight (fig. 1). The rays are generated at 45 kilovolts, 2 milliamperes. The target is 1.8 cm. from the face of the tube. Consequently, when the tube is brought into direct contact with a lesion, the target-skin distance is only 1.8 cm. By virtue of the inverse square law, the intensity of radiation at this point is far greater than that of the usual types of apparatus, which

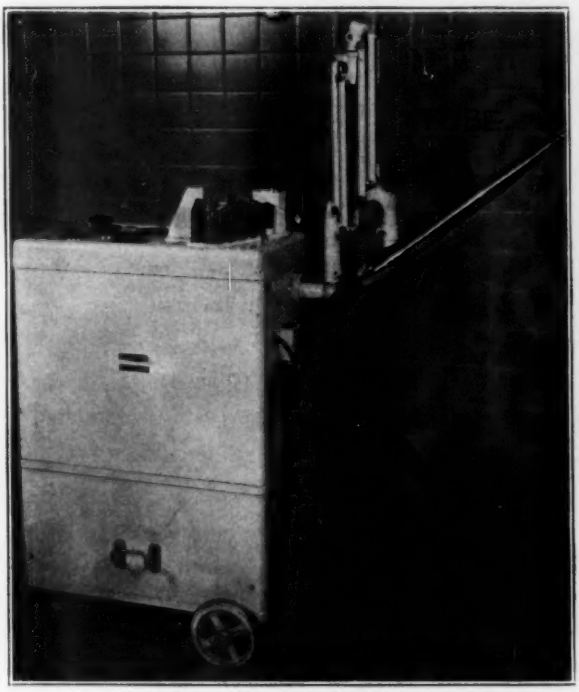

Fig. 1.—Contact therapy unit, air-cooled type.

are used at a target-skin distance of 30 to 50 cm. The present output of our unit is 10,000 r in forty-eight seconds. The dosage gradient in the tissues is steep, since the intensity falls off rapidly as the distance increases. Only a small percentage of the rays penetrate to any great distance. The accompanying table gives the output of our unit and the percentage of depth dose at 1 and at 5 cm. The tube is usually used without filtration, but aluminum filters of 1 and 2.5 mm. may be added. Metal cones with openings of various sizes are furnished; these may be used to cap the tube head and limit the diameter of the

irradiating field. Some of the cones have tips 2 cm. in length, which increase the target-skin distance 1.8 to 3.8 cm. The rays can be aimed into an even narrower angle with a tip of smaller diameter (fig. 2 *A*) than with the tube itself. Some of the tips leave the face of the cone at an angle and permit the turning of the cone in such a direction as to furnish protection to neighboring structures (fig. 2 *B*).

TREATMENT OF LESIONS VARIOUSLY LOCATED

Lesions Located at the Inner Canthus.—These lesions are often difficult to treat because of their inaccessible location—beneath an overhanging brow and to one side of the nasal ridge. The patient is seated in a dental chair, in a good light, with the head fixed to the head rest. A tube cap is chosen so that the smallest field is used which will

Fig. 2.—*A*, a cone with a tip which can fit into the canthus is added to the tube. *B*, a tip which leaves the cone at an angle permits treatment of an eyelid while the vital neighboring structures are protected.

Calibration of the Contact Therapy Machine Which Indicates Its Output in Roentgens

Filter: Aluminum, Mm.	Focal Skin Distance, Cm.	Time in Minutes and Seconds to Deliver Dose Indicated		r per Minute in Air	Depth Dose at 1 Cm. (5 Cm.), %
		r, 10,000	r, 1,000		
0	1.8	0′48″	0′4.8″	12,600	23 (0.6)
	2.0	(1′22″)	(0′8.2″)	1,350	
	3.8	3′32″	0′21.3″	2,820	36 (1.9)
1	2.05	5′43″	0′34″	1,750	36 (1.9)
	4.05	22¼′	2′14″	449	51 (4.9)
2.5	2.05	14½′	1′27″	693	40 (3.0)
	4.05	56¼′	5′37″	178	57 (7.0)

completely encircle the lesion and include a small areola of normal tissue. If the head of the tube is too large to fit into the irregular

space and cannot come into contact with the lesion, a smaller cone is added, which increases the target-skin distance from 1.8 to 3.8 cm. but can reach a smaller cavity. At a target-skin distance of 1.8 cm. no filter is used. Approximately 10,000 r is given in forty-eight seconds, and this amount is usually sufficient to eradicate a skin carcinoma. When the target-skin distance is increased to 3.8 cm., divided doses are given, 6,000 to 8,000 r at one sitting. A mild edema appears almost immediately after the treatment. The next day a well demarcated erythema, localized to the area exposed, is noted. The erythema deepens to tanning, and later a superficial crust forms. In four to six

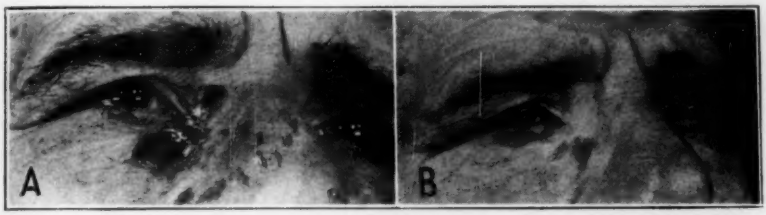

Fig. 3.—*A*, long basal cell epithelioma which received three treatments of 13,000 r each within six weeks. Five months later a small recurrent lesion was treated with 10,000 r. *B*, the end result, over one year later.

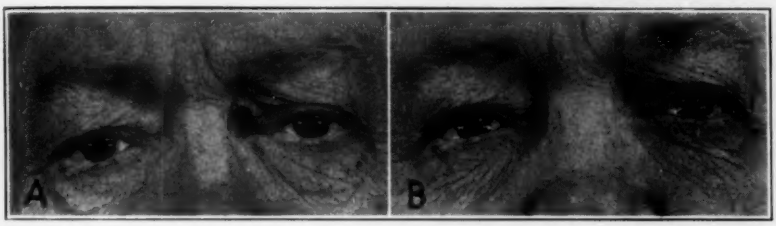

Fig. 4.—*A*, basal cell epithelioma at the inner canthus to which one treatment of 13,000 r was administered (one minute). *B*, the end result three months later.

weeks the crust falls off, and a new, pliable scar remains. The lesion occasionally recurs at the periphery of the irradiated area and must be retreated with care to prevent overexposure of the already exposed port. Overtreatment may result in delayed healing. Figures 3 and 4 illustrate some of the results obtained.

Many lesions are located low in the canthus and over the naso-lacrimal duct. Fibrosis or direct involvement has often resulted in ductal stenosis with excessive tearing (as in the patient shown in figure 3). The end result of the therapy, likewise, may augment the stenosis. When this happens the ophthalmologist at the Brooklyn Cancer Institute dilates the duct with good results. A mild degree of conjunctivitis

or tearing may be seen as other complications, but these are transient. Because the rays are aimed away from the essential ocular structures, late complications are not anticipated.

Lesions on the Lid.—Lesions on the lid are usually located at the edge and over the eye itself. The problem of shielding is always a factor, and surgical intervention is often resorted to in an effort to avoid complications from irradiation. In the technic under discussion a cone is chosen which leaves the face of the tube at an angle and permits the aiming of the rays away from the eye (fig. 2 *B*). The lesion is usually on the lower lid, which may be everted downward away

Fig. 5.—*A*, basal cell epithelioma involving the outer canthus and over half of the lower lid. *B*, the end result of treatment with the divided dose technic (1,000 r given daily for ten treatments).

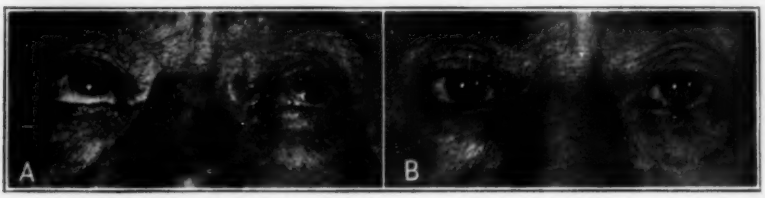

Fig. 6.—Epithelioma of the bulbar conjunctiva of the left eye. The lesion extended from the inner angle of the eyeball to near the iris. *B*, after irradiation.

from the eye, either with the finger or with adhesive tape. The treatment is given in a very short time, and the position may be held without movement. If the distance is 1.8 cm., between 5,000 and 10,000 r is given at one sitting. The reaction is like that in other locations. Loss of eyelashes is to be expected, but the total cosmetic result is excellent (fig. 5). The need for surgical intervention is usually obviated.

Lesions of the Conjunctiva.—These are rare. In a large service we have seen only one squamous cell carcinoma in this location in over three years. However, the method lends itself to the treatment of such lesions, since most of the rays are absorbed superficially. One patient (fig. 6) was treated with a water-cooled type of apparatus.

The eye was anesthetized with 1 per cent butyn sulfate, the tube was placed in direct contact with the lesion and 10,000 r was delivered in one application. This patient was treated without fixation of the eyeball, but, even though the irradiation was successful, we would recommend fixation of the globe in the treatment of such lesions. Eighteen months after therapy there had been no evidence of recurrence or complication.

Lesions Elsewhere About the Eye.—These lesions are usually basal cell carcinoma and are given 10,000 to 13,000 r by close range therapy in one sitting. Crusting as an end result of the radiation reaction usually persists for six to eight weeks, but the lesion is usually eradicated. Large superficial lesions are treated by cross fire from two or three angles. When the technic under discussion is carried out, 1,000 r is delivered to each area daily for a total of 6,000 to 10,000 r per area.

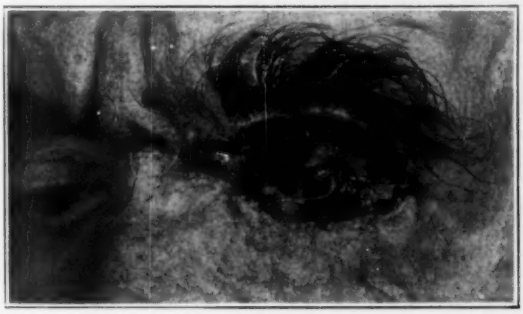

Fig. 7.—Basal cell epithelioma involving both lids and the orbit. This lesion was not suitable for contact therapy. (The orbit was exenterated and a radium pack was used.)

The tumor dose to any one point is calculated not to exceed 18,000 r. The divided dose technic permits more complete control of the tumor and of the radiation reaction and thus allows the therapeutist an opportunity to modify his dosage.

LIMITATIONS OF THIS THERAPY

It is to be remembered that this type of therapy is applicable only to superficial lesions, since most of the roentgen energy is expended in the first few millimeters of tissue. While this characteristic is utilized advantageously in the treatment of most lesions about the eye, the technic should not be used for lesions which are widely invasive or located deeply in the eye itself (fig. 7). Likewise, lesions which invade the bony orbit had best be treated by some other technic. Infants, patients with tremor or patients who cannot be made to understand

that they must not move during the treatment cannot be treated by this method, since slight movement results in the radiation being focused off to one side. This may be dangerous, since the cornea and other delicate intraocular structures may be injured.

SUMMARY

The contact type of roentgen ray therapy is of particular advantage in the treatment of superficial malignant lesions about the eye, because:

1. The small shock-proof tube permits ease of application and protection of vital ocular structures.

2. Inaccessible lesions, such as those deep in a canthus, may be reached without injury to surrounding overhanging structures.

3. The cosmetic results are excellent. No late injuries due to the radiation have been observed.

The method is comparatively new. The dosage should be considered tentative, although we have had minimal complications using the technic as outlined.

Brooklyn Cancer Institute, Clarkson Avenue.

THROMBOPHLEBITIS OF THE CAVERNOUS SINUS

A REVIEW OF REPORTED RECOVERIES WITH SPECIAL REFERENCE TO THROMBOPHLEBITIS OF STAPHYLOCOCCIC ORIGIN

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In selecting for discussion particular groups of severe staphylococcic infections according to anatomic divisions, we have been guided largely by practical consideration to present first reports on patients with disorders commonly regarded as highly lethal. Observations on such patients and especially presentation of the records of those in whom recovery has occurred may be of immediate aid to physicians confronted with similar desperate clinical problems. One such clinical entity which physicians may well regard as a challenge to their most diligent efforts is staphylococcic septic thrombosis of the cavernous sinus, its tributaries and communications.

The present paper concerns certain aspects of thrombophlebitis of the cavernous sinus, particularly the anatomic structure of this venous plexus, the causation and mode of its infection and recorded cases in which the patient has recovered. Consideration of a series of original cases will follow in another paper.

ANATOMIC CONSIDERATIONS

The two cavernous sinuses are situated between folds of the dura mater at the base of the skull, one on each side of the sella turcica. Each sinus is about 20 to 25 mm. in length and about 10 mm. in diameter, is roughly and irregularly quadrilateral in cross section and extends from the sphenoid fissure to the apex of the petrous pyramid. To avoid confusion it may be well at the outset to distinguish clearly between the structural character of the cavernous sinus and that of other large dural sinuses, such as the transverse or the lateral sinuses. The latter are simple large venous channels enclosed within the dural membrane. The cavernous sinus is also enclosed within the dura, but

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it is not a simple venous channel. It may be more properly regarded as a mass of rather loose connective tissue enclosed in the firmer dura and containing in its substance a large artery, several nerves and a rich plexus of anastomosing venous channels. The precise relation of these contained structures varies at different levels, but in general it may be said that the third and fourth cranial nerves course through the cavernous sinus close to the dura on its upper lateral surface; the first, or ophthalmic, division of the fifth nerve, slightly below the fourth nerve, and the second, or maxillary, division of the fifth nerve, just below and slightly laterad to this. The sixth cranial nerve is more deeply situated, mesial to the first division of the fifth nerve. The carotid artery lies nearer to the central region of the sinus mesial to the fourth nerve and above the sixth nerve. The venous channels are numerous and for the most part of less cross section area than the carotid artery. They are generally distributed through the substance of the sinus structure but are largest and most numerous below the carotid artery and in the mesial portion of the sinus near the sella turcica and the pituitary body. Turner and Reynolds[1] have clearly demonstrated these relations and the important distinction between the structural character of the so-called cavernous sinus and that of the other dural venous sinuses, a distinction sometimes not adequately emphasized by the authors on surgery who discuss this region. This anatomic structure renders attempts at surgical drainage of doubtful value.

The venous plexus within the cavernous sinus receives, at its anterior end, the central vein of the retina and the superior and inferior ophthalmic veins, thus draining the eyeball, the orbital tissues, the ethmoid tissues and the eyelids. A large communication between the superior ophthalmic and the angular vein provides an important connection with the anterior facial vein and its anastomoses, devoid of valves. The sphenoparietal sinus of the dura, draining the meninges, the inferior-anterior portion of the cerebrum and the diploe of the cranium in this region, also forms an important tributary of the cavernous venous plexus at its anterior end. The venous channels of the two cavernous sinuses are connected by large anterior and posterior intercavernous venous channels, which pass in front of, beneath and behind the hypophysis cerebri to form a complete venous circle around it. Posteriorly the cavernous plexus is directly continuous with the carotid venous plexus, which surrounds the carotid artery in the carotid canal of the

1. Turner, A. L., and Reynolds, F. E.: (*a*) Furuncle of the Right Nasal Vestibule with Septic Thrombosis of the Cavernous Blood Sinuses: Leptomeningitis; Death; Autopsy, J. Laryng. & Otol. **41**:73-86, 1926; (*b*) Intracranial Pyogenic Diseases, London, Oliver & Boyd, 1931.

temporal bone, receives veins from the middle ear and terminates below in the internal jugular vein. At the apex of the petrous bone the relatively straight and simple superior and inferior petrosal sinuses extend from the posterior end of the cavernous plexus backward to the transverse venous sinus and to the jugular bulb, respectively. Their anterior ends mark approximately the transition from the cavernous plexus to the carotid plexus. There are also communications with the pterygoid plexus. These multiple connections are shown in the accompanying illustration, taken from Turner and Reynolds.[1b]

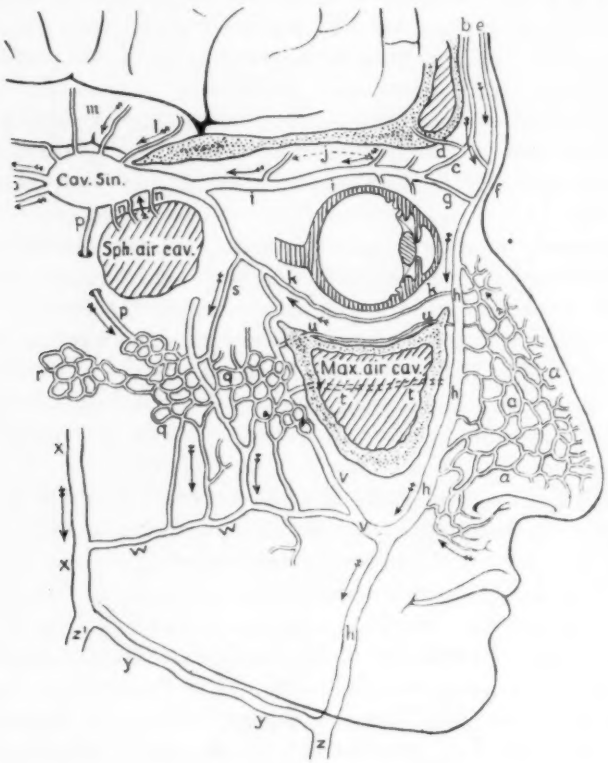
The carotid artery imparts its pulsation to the venous blood in the carotid plexus and the cavernous plexus, and this pulsation is doubtless an important factor in the movement of the blood within these venous channels.

The anatomic structure and the relations of the cavernous plexus are such that its blood may normally flow backward through the petrosal sinuses and the carotid plexus. However, the current may be deflected forward toward the angular and the facial vein, downward to the pterygoid plexus or laterally across to the cavernous plexus of the other side, or the blood may remain relatively stagnant. An inflammatory process may change the pressure relations so that the flow of venous blood is impeded and becomes directed away from the inflamed area, even in a direction opposite to that of the normal current. Blocking of the left jugular bulb, for example, allows blood from the mastoid process and the middle ear to pass along the petrosal sinuses to the left cavernous plexus and through the intercavernous connections to the right cavernous plexus. In the reverse direction, inflammation and swelling of the face obstruct the exit through the facial vein and allow the blood in the angular vein to pass backward into the ophthalmic veins and the cavernous plexus, where the slow current may favor the formation of a clot. Hence a purulent inflammation of the face, particularly in the area above the level of the mouth, presents grave possibilities. When in the course of such an inflammation there is rapidly developing edema of the eyelids, a partial obstruction of the venous plexus of the cavernous sinus, with extension of the thrombosis forward into the ophthalmic veins, should be suspected. Rapid advancement of the edema, with exophthalmos, followed by similar signs in the fellow eye after twelve to forty-eight hours, completes the clinical picture of venous obstruction in the cavernous sinuses.

CAUSATION AND SOURCES OF INFECTION

Thrombosis of the venous channels of the cavernous sinus has been observed in general marasmus and as a result of local physical injury by violence or by tumor growth. With such thrombosis we are not here concerned. For the most part clotting of the blood in these channels is initiated by a bacterial inflammation at some place in the head or pos-

sibly in the neck. The common locations of the inciting lesion are in the auditory apparatus; the nasal passages and the nasal accessory air cavities; the pharynx, mouth and teeth, and the skin of the head and neck, more especially the skin near the lips or the nasal vestibule. All these regions are connected with the cavernous sinus by venous chan-



Diagrammatic representation of the afferent and efferent venous channels of the cavernous sinus (from Turner and Reynolds[1b]): *a*, subcutaneous venous plexus; *b*, supraorbital vein; *c*, communicating vein between the supraorbital and the superior ophthalmic vein; *d*, frontal diploic vein; *e*, frontal vein; *f*, angular vein; *g*, communicating vein between the angular and the superior ophthalmic vein; *h*, anterior facial vein; *i*, superior ophthalmic vein; *j*, anterior and posterior ethmoid veins; *k*, inferior ophthalmic vein; *l*, sphenoparietal blood sinus; *m*, superficial inferior cerebral veins; *n*, veins from the mucosa of the sphenoid air cavity; *o*, superior and inferior petrosal sinuses; *p*, vein of Vesalius to the pterygoid venous plexus; *q*, pterygoid venous plexus; *r*, pharyngeal venous plexus; *s*, communication between the inferior ophthalmic vein and the pterygoid plexus; *t*, sphenopalatine vein from the nasal mucosa to the pterygoid plexus; *u*, intraorbital vein to the pterygoid plexus; *v*, deep facial vein joining the anterior facial vein; *w*, internal maxillary vein joining the posterior facial vein; *x*, posterior facial vein; *y*, anterior division of the posterior facial vein joining the anterior facial vein; *z*, common facial vein entering the internal jugular vein; z^1, posterior division of the posterior facial vein to form the external jugular vein.

nels permitting passage of blood to the sinus. Evidently the thrombus is sometimes propagated along the lumen of a tributary, to reach the cavernous plexus by continuous extension. This process has been observed in otitis media and in mastoiditis, the clot being propagated along the petrosal sinuses or the carotid plexus, and in severe inflammations of the ethmoid and sphenoid air cavities, in which the thrombus may extend by continuity through venules in the bony floor of the skull to reach the cavernous sinus. A thrombus may come from the pterygoid plexus in the same manner. The clot may be infected with bacteria at the time of its formation, but in some cases it appears to be infected only at the end next to the focus of severe inflammation. In these instances it may be free from bacteria in the cavernous plexus, and, although it obstructs the flow of blood, it may then be regarded as protective rather than a menace. Unless the original infection is overcome, such an aseptic clot tends to become infected if the patient survives long enough. A second and more malignant type of thrombosis is the discontinuous form, in which the original lesion, for example a carbuncle on the lip, is not connected to the cavernous sinus by a continuous thrombus. The blood flowing from the carbuncle carries toxic substances, which induce swelling of the endothelial lining of the tortuous venous channels of the cavernous sinus, and bacteria traveling free in the blood plasma or within the bodies of wandering leukocytes are caught by the softened, swollen endothelial cells and by the clumps of platelets adhering to them, thus initiating a thrombus which is infected at its beginning. This theoretic picture of events is in accord with the direct observations of Turner and Reynolds on the venules about a carbuncle of the lip and on the venous channels of the cavernous sinus itself and is analogous to the observations of one of us [2] on septic pylephlebitis secondary to suppuration of the appendix or the gallbladder. Such an infected thrombus tends to extend into all the connecting venous channels and to give off bacteria to the circulating blood at its surface. The infection tends to spread through the walls of the thrombosed vessel, to set up purulent inflammation of the contiguous structures. Hence, there may develop leptomeningitis, brain abscess, osteomyelitis of the skull, orbital abscess, pachymeningitis or epidural abscess. The infecting micro-organism is usually the hemolytic streptococcus when the primary disease is acute otitis media and the staphylococcus when the primary lesion is a furuncle of the nasal vestibule, lip or other area of the skin. When the infection originates in the nasal accessory air cavities or in the pharynx, these bacteria are also found, but in addition others must be considered, particularly the pneumococcus and Pfeiffer's bacillus.

2. MacNeal, W. J.: Structural Changes in the Appendix, Gall Bladder, and Liver from the Same Patient, The Beaumont Foundation Lectures, Third Series, St. Louis, C. V. Mosby Company, 1924, pp. 68-164.

PROPHYLAXIS OF STAPHYLOCOCCIC SEPTIC THROMBOSIS

The care given to the relatively common pimples and boils on the face seems to be of greatest significance in avoiding the highly malignant extension to the cavernous sinus. Almost invariably, suitable inquiry of the unfortunate patient will disclose a history of meddling therapy, amateur or professional, in the form of squeezings, incisions or applications of radiant energy. We have dealt with many examples of furunculosis of the face in the past ten years, and, so far, local rest and application of moist heat to the lesion, coupled with the intravenous use of staphylococcus bacteriophage, have been followed in every case by healing of the lesion without extension of the infection to the intracranial venous sinuses.

HISTORICAL ACCOUNT

The earliest description of thrombophlebitis of the cavernous sinus seems to be that of Duncan [3] published in 1821:

The patient was a robust mason aged 45 with intermittent purulent discharge from the left ear since 1800. About Nov. 4, 1820 a constant pain in the left side of the head developed, and there was discharge of thick pus from the left ear, now totally deaf. On November 11 the patient came under observation. On November 18 there was violent persistent pain over the eyes. Venesection on November 21 yielded 16 ounces (473 cc.) of blood which was "much buffed." Some days before death the patient ceased to complain of headache and referred all his pain to the left side of the neck, where the skin was red and tense. Incision below the mastoid evacuated blood, pus and air in abundance. The patient became delirious and died on November 30. At autopsy slight effusion below the arachnoid was observed; the left hemisphere was livid, soft and dark when incised; "the cavernous sinuses were filled with matter of a gray colour"; the body of the sphenoid was carious, especially toward the left, and a probe could be passed through it backward into the petrous bone.

Bright [4] has given a classic account of another case:

George Botwell, aged 42, was admitted to the hospital on May 25, 1829 with lacerations over both eyebrows and over the right zygoma, and with several fractured ribs, having been kicked and trampled by a horse, while intoxicated. He was treated by bleeding until syncope occurred, administration of mild mercurous chloride in doses of 8 grains (0.5 Gm.), strapping of the chest wall and multiple punctures of the side to let out the confined air. He was convalescent on June 10 and on June 14 absconded, to return again the same evening, apparently intoxicated. Bleeding and purgation again were followed by improvement. During the night of June 15-16 he had rigors for the first time, and on the morning of June 16 he was incoherent and there was observed slight protrusion of the globe of the right eye. Resort was had to further bleeding and purgation (mild mercurous chloride, 8 grains). On June 17 there were greater protrusion of the right eyeball and dilatation of the left pupil.

3. Duncan, A.: Contributions to Morbid Anatomy: No. II, Edinburgh M. & S. J. **17**:319 (July 1) 1821.

4. Bright, R.: Diseases of the Brain and Nervous System, in Reports of Medical Cases, London, Longman [and others], 1831, vol. 2, pt. 1.

At autopsy, on June 18, there were observed partial necrosis of the frontal bone, epidural abscess compressing the frontal lobe, slightly milky fluid in the ventricles and puriform lymph over the anterior face of the cerebellum and along the optic nerves. On the cerebrum and the cerebellum there were veins distended with pus. The right orbital veins were likewise distended with pus. The cavernous sinus on each side was full of pus.

Abercrombie, who is sometimes credited with the first recorded description of thrombosis of the cavernous sinus, mentioned in his paper published in 1818 [5] the case of Miss S., aged 16, who died Aug. 12, 1816. At autopsy the left lateral sinus when compressed discharged purulent matter and some thick cheesy matter. It contained no blood, and its coats were much thickened. There was no mention of the cavernous sinus in this case, nor have we been able to find any mention of thrombosis of the cavernous sinus in the paper. In his book, the first edition of which appeared in 1828,[6] there is an account of the same patient, again without mention of the cavernous sinus. However, in the third Edinburgh edition and in the second American edition, after the account of the identical patient there is an added paragraph which contains this statement: "Dr. Bright found the lateral, cavernous, and petrosal sinuses of the left side, full of dark, ill-conditioned pus, which also filled the jugular vein, as far as its junction with the subclavian." It is evident that this statement does not relate to the autopsy on Miss S., aged 16, who died Aug. 12, 1816, but in any event its publication appears to have been preceded by the reports of Duncan and of Bright, already mentioned.

The classic description of the disease from the viewpoint of the ophthalmologist, by H. Knapp,[7] came much later, in 1868.

Therapeutic efforts have been varied, and the success of any particular procedure has, so far, not been frequent enough to establish it as a standard treatment.

Bircher [8] reported the first recorded instance of recovery of a patient with thrombosis of the cavernous sinus following a surgical procedure:

Rosa Humm, aged 25, had undergone a mastoidectomy on the left side on Sept. 8, 1893. There was oculomotor weakness of the left eye on September 16

5. Abercrombie, J.: Observations on Chronic Inflammation of the Brain and Its Membranes, Edinburgh M. & S. J. **14**:265-328 (July 1) 1818.

6. Abercrombie, J.: Pathological and Practical Researches on Diseases of the Brain and the Spinal Cord, Edinburgh, Waugh & Innes, 1828; Second American Edition from the Third Edinburgh Edition, Enlarged, Philadelphia, Carey, Lea & Blanchard, 1836.

7. Knapp, H.: Ueber Verstopfung der Blutgefässe des Auges, Arch. f. Ophth. (pt. 1) **18**:207-251, 1868.

8. Bircher, H.: Phlebitis des Sinus transversus, petrosus inferior und cavernosus. Eröffnung und Disinfektion nach Entfernung der Felsenbeinpyramide. Heilung, Centralbl. f. Chir. **20**:483, 1893.

and fixation of the left globe on September 19. On September 20 the skull was entered above the left auditory canal, the floor of the middle fossa being exposed. The petrous pyramid was chiseled away except the lower wall of the carotid canal. Just posterior to the apex of the pyramid, Bircher came on a gray focus, from which foul pus was evacuated. This lesion was opened with a sharp curet and irrigated with mercury bichloride solution. The wound was packed with antiseptic gauze. The anatomic diagnosis was purulent inflammation of the sinus transversus from the site of the mastoid emissary vein, extending through the inferior petrosal sinus to the posterior end of the cavernous sinus. No bacteriologic studies were recorded. The patient survived, with paralysis of the left facial nerve and light perception in the left eye.

Operative attack directly on the cavernous sinus itself was carried out by Hartley in consultation with Knapp [9] in a case of neoplastic obstruction of the sinus. The patient survived for about six weeks, finally dying of extension of the sarcoma.

Dwight,[10] in collaboration with Germain, operated by the Krause technic through a temporal bone flap, elevated the temporal lobe of the brain and incised the cavernous sinus, obtaining a free flow of dark, semiclotted blood. Gauze packing readily controlled the bleeding. The operative time was only eight minutes. The proptosis, which had been marked, improved at once and had practically disappeared in half an hour. The patient lived for six and one-half hours after the operation.

Reported Recoveries.—In addition to the case of Bircher mentioned, the following cases may be mentioned without our pretending to offer a complete list of all reported recoveries:

Parkin [11] reported on a boy of 9 years who had a running ear for two weeks, for which a mastoidectomy and ligation of the jugular vein were done. Three weeks later there was a recurrence of fever with edema of the eyelids, suggesting thrombosis of the cavernous sinus. This subsided and the patient recovered.

Cohen-Tervaert [12] reported the recovery of a 16 year old boy who had a history of chronic otorrhea:

After an exacerbation of symptoms there occurred the classic signs of thrombosis of the cavernous sinus involving the left eye. Schwartze's operation, including

9. Knapp, H.: A Case of Traumatic, at First Doubtful, Orbital Sarcoma, Followed by Aseptic Thrombosis of the Cavernous Sinus: Successful Sinus Operation by Dr. Frank Hartley; Death Later by Extension of the Pseudoplasm; Autopsy; Remarks, Arch. Ophth. **29**:463-475, 1900.

10. Dwight, E. W., and Germain, H. H.: Thrombosis of the Cavernous Sinus, with Report of Four Cases, Including One Cranial Operation, Boston M. & S. J. **146**:456-461 (May 1) 1902.

11. Parkin, A.: Two Cases of Aural Pyemia Treated by Operation, Lancet **1**:522 (March 11) 1893.

12. Cohen-Tervaert, G. D.: A Case of Thrombosis of Both Sinus Cavernosi, as a Complication of Chronic Mastoiditis, ex Otorrhea, Which Ended in Recovery, Internat. Otol. Cong. (1899) **6**:446-451, 1900.

an opening of the lateral sinus, was performed without immediate recession of the ocular symptoms. There followed a stormy course during which the left eye, which had become almost normal, again was involved, and some time later the right eye showed chemosis and exophthalmos. Repeated and extensive surgical ventures were carried out, including one exploratory craniotomy. Improvement began twenty-six weeks after onset of the illness, and the progress was steady. The only residual was partial loss of vision in both eyes.

Stocker [13] observed the following case:

A woman of 48 years had a laceration at the outer angle of the left eye due to an injury which had occurred on Jan. 14, 1895. On January 20 there were proptosis, chemosis and a temperature of 39 C. (102.2 F.). On January 22 an incision was made at the outer canthus, 3 cm. in length, through conjunctiva, skin and fascia down to the bone, and the wound was enlarged by blunt dissection along the outer orbital wall and irrigated with warm 1:2,000 solution of mercury bichloride. A drain of iodoform gauze was inserted. On January 23 the right eye was proptosed so that it was not covered by the lids, and the globe was almost fixed; chemosis was present, and the temperature was 39.2 C. (102.56 F.). Improvement was evident on January 25, and the patient recovered, with good vision in the right eye and slight peripheral vision in the left eye. The patient died in 1899.

Stocker called this a typical example of thrombosis of both cavernous sinuses with recovery following correct, early surgical treatment. His claim has been disputed by Stower,[14] who expressed the belief that the incision had no influence.

In 1902 Day [15] reported a case of cavernous sinus thrombophlebitis in a boy of 11 years who had had chronic otitis media. After a mastoidectomy and incision into a pus pocket in the neck, there were exophthalmos and proptosis in the left eye followed in thirteen days by involvement of the right eye. Exploratory incision into the orbit yielded negative results. The patient recovered but was totally blind.

Hildebrand [16] reported the case of a man in whom there developed chills, fever, proptosis, edema of the lids and fixation of the eyeball two days after cauterization of the nasal septum. Tavel's antistreptococcus serum was injected into both forearms and into the thigh. The patient recovered. Hildebrand was not certain that the serum caused the recovery but stated the belief that it should be used in such cases. The bacteriologic causation was not determined.

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13. Stocker, F.: Ein seltener Fall von Thrombosirung der vordern basalen Hirnsinus, im Auschluss an orbitale Thrombophlebitis, Arch. f. Augenh. (supp.) **44**:105-146, 1901.

14. Stower, P.: Zur Behandlung der septischen Thrombose des Sinus cavernosus orbitalen Ursprungs, Klin. Monatsbl. f. Augenh. **45**:147-157 (Aug.) 1907.

15. Day, E. W.: Supposed Cavernous Sinus Thrombosis, Ann. Otol., Rhin. & Laryng. **11**:520, 1902.

16. Hildebrand: Heilung einer rhinogenen Thrombose des Sinus cavernosus, Verhandl. d. deutsch. Gesellsch. f. Chir. **33**:105-107, 1904.

Signard [17] in 1904 reviewed 43 cases of thrombosis of the cavernous sinus, including that reported by Cohen-Tervaert and 3 others in which recovery occurred, in all of which the thrombosis followed chronic otitis media. In Brieger's patient, a 22 year old man, the classic ocular symptoms developed nine days after he had been hospitalized for treatment of an ocular infection. A mastoid operation was accompanied by severe hemorrhage. On the first postoperative day the ocular symptoms began to recede. Recovery was rapid and uneventful. Preysing's patient was a girl of 13 with a history of otorrhea of six years' duration. A radical mastoidectomy, performed to relieve an exacerbation of symptoms, was followed by diplopia and exophthalmos on the left side. The right eye was not involved. Deafness developed as the ocular symptoms receded. The patient remained deaf. The third patient, that of Bezold, was reported on as follows:

> A veterinary medical student aged 19, who had suffered for fifteen days with an infection of the left ear, was admitted to the hospital Aug. 19, 1898 with a temperature of 39.4 C. (102.92 F.) and inflammation of the apophysis of the left mastoid. There was a large, tender and inflamed gland at the retromaxillary fossa. The mastoid was opened August 29. Granulation tissue extended to the sigmoid sinus, which was opened for 2 cm. The superior part was normal and bloody, but below it was yellow and covered with a deposit of fibrin. The operation was stopped because of hemorrhage from an emissary vein. A short period of improvement was succeeded by an elevation of the temperature to 40 C. (104 F.) about September 6. Chills occurred on September 7, 8 and 9, and the purulent exudate from the mastoid wound became sanguinous. The optic papillae were poorly defined on both sides and were slightly red. Paralysis of the sixth cranial nerve, with diplopia, was present. The sigmoid sinus was opened September 9, and pus was found. The following day the temperature returned to normal, and recovery was gradual.

Werner [18] presented a case in 1905 in which the diagnosis may be open to question. The patient, a boy of 6 years, showed pronounced exophthalmos of the right eye, with edema of the lids, on the ninth day following the onset of mild scarlatina. The proptosis and edema gradually subsided, the eye returning to normal in about two months. The left eye did not become involved. In the discussion of Werner's paper, Dr. Marshal Day, of Dublin, stated that he had seen 2 patients with similar complications following scarlatina, one making an eventual recovery and the second dying after the appearance of the ocular symptoms. Sidney Phillips, of the London Fever Hospital, stated that

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17. Signard, H.: Contribution à l'étude de la thrombo-phlébites des sinus caverneux d'origine otitique, Thesis, Paris, no. 339, 1904.

18. Werner, L.: Unilateral Proptosis and Edema of the Lids (? Thrombosis of the Cavernous Sinus) Occurring in the Course of Scarlatina, Ophthalmoscope **3**:222 (May) 1905.

he had seen 3 patients with unilateral edema of the eyelids following scarlatina. The edema was associated with otitis media and improved concurrently with it. All 3 patients recovered; an abscess formed about the eye of 1 before recovery. Dr. Phillips attributed the orbital complications to thrombosis of the cavernous sinus, and Dr. Werner stated the belief that this explanation fitted his case better than that of localized cellulitis.

Seggel [19] reported the case of a soldier who had headache and tonsillitis followed by disturbed vision in the right eye on Nov. 15, 1899, with chills and vomiting; proptosis, chemosis and protrusion of the conjunctiva of the right eye, and a temperature of 40.5 C. (104.9 F.). On November 20 the left eye became blind. The proptosis and chemosis subsided, and the patient recovered after several months of expectant treatment, with total loss of vision.

Coffin [20] saw a woman aged 59 with frontal headache on the right side, nausea, vomiting, bulging of the right eye, diplopia and mild fever. After ten days a complete Killian operation was performed, which revealed congestion of the frontal and ethmoid sinuses. The patient recovered. Coffin expressed the belief that the radical Killian operation is justified in the treatment of thrombosis of the cavernous sinus when no diseased focus can be found elsewhere than in these sinuses.

Adair-Dighton [21] reported the following case:

> A girl of 13 had had otitis media since December 1911. A radical mastoidectomy was done on Feb. 17, 1912. On February 26 there was a chill, and on the next day the internal jugular vein could be palpated, the right eye protruded, the right upper lid drooped and there was a dusky haze around the left eyelids. On this day the internal jugular vein was ligated and excised up to the level of the mastoid; the lateral sinus was opened, curetted and irrigated. Polyvalent streptococcus serum was administered. The patient improved at once, and all signs of obstruction of the cavernous sinus had vanished in two days.

A case of recovery from thrombosis of the cavernous sinus was reported by Johnson [22]:

> The patient, a man of 59, showed chemosis and exophthalmos of the left eye associated with the appearance of acute sepsis twelve days after a mastoidectomy. After the removal of a clot from the sigmoid sinus and ligation of the internal jugular vein, which was curetted toward the torcular without yielding

19. Seggel, K.: Erblindung infolge Tonsillitis phlegmonosa auf dem Wege der Thrombosinusitis cerebralis, Klin. Monatsbl. f. Augenh. **45**:129-147 (Aug.) 1907.

20. Coffin, L. A.: Cavernous Sinus Thrombosis, Ann. Otol., Rhin. & Laryng. **18**:786-788 (Dec.) 1909.

21. Adair-Dighton: Cavernous Sinus Thrombosis of Otitic Origin: Recovery, Ann. Otol., Rhin. & Laryng. **21**:411-413, 1912.

22. Johnson, H. R.: Case of Cavernous Sinus Thrombosis of Otitic Origin, with Recovery, Laryngoscope **23**:134 (Feb.) 1913.

a flow of blood, the ocular signs gradually subsided. Vision was completely lost owing to optic nerve atrophy. The infective organism was a streptococcus.

Barnhill [23] reported a case in which a mastoidectomy was performed. Later an extensive operation was done on the lateral sinus, which was full of pus. After the patient's doing well for some time, classic signs of thrombosis of the cavernous sinus developed on the right side only. The patient was sent home and was able to be up and about, the ocular signs having disappeared, but died suddenly two months later, apparently from embolism.

Langworthy [24] proposed an operation through the nose, in which the surgeon would remove the middle turbinate and the ethmoid labyrinth to enter the sphenoid sinus and then break through the wall of the sphenoid air cavity to enter the cavernous sinus. By correspondence he learned of 3 recoveries from septic thrombosis of the cavernous sinus: 1 in a case of R. P. Scholz, in which thrombosis occurred after radical mastoidectomy and ligation of the jugular vein; 1 in a case of A. B. Kanavel, in which it occurred after local drainage of an infection of the neck, and the third in a case of A. E. Halstead, in which it originated after operation on the ethmoid and the patient recovered with expectant treatment. Of the twenty-one general surgeons responding to his questionnaire, none had ever attempted a direct operation on the cavernous sinus.

Chisolm and Watkins,[25] in a study of 50,000 surgical cases, found only 8 instances of thrombosis of the cavernous sinus, and they added 4 more from other services. One patient survived:

He was admitted on Aug. 5, 1916 with swelling of the right eye and the right side of the face, ascribed to swimming and diving on July 29. On August 7 a tooth was extracted and the maxillary antrum was punctured. A diagnosis of thrombosis of the cavernous sinus was made on August 11. Blood taken for culture on August 16 yielded five colonies of Staphylococcus aureus per cubic centimeter of the patient's blood. Surgical intervention was refused by the parents and was not urged because of the essentially bad prognosis. Staphylococcus vaccine was given on August 23 and 27 and on September 3, 13 and 18. On October 9 a sequestrectomy was performed for osteomyelitis of the skull. At this time the left patella was removed. The patient was discharged November 24, with residual osteomyelitis of the left leg. He was in good general health in May 1920.

23. Barnhill, J. F.: Report on a Case of Sinus Thrombosis with Extensive Operation on the Sinus and Jugular Vein in Which Symptoms of Cavernous Sinus Thrombosis Developed Followed by Apparent Recovery but with Ultimate Death, Ann. Otol., Rhin. & Laryng. **23**:386, 1914.

24. Langworthy, H. G.: Anatomic Relations of the Cavernous Sinus to Other Structures, with Consideration of Various Pathologic Processes by Which It May Become Involved, Ann. Otol., Rhin. & Laryng. **25**:554-586 (Sept.) 1916.

25. Chisolm, J. J., and Watkins, S. S.: Twelve Cases of Thrombosis of the Cavernous Sinus: From a Study of Fifty Thousand Surgical Histories in the Johns Hopkins Hospital, Arch. Surg. **1**:483-512 (Nov.) 1920.

Friedmann,[26] in an important paper warning against the uncritical appraisal of remedies for sepsis, reported the following case:

A man aged 26 was admitted Dec. 13, 1921 with a carbuncle on the left side of the upper lip. A blood culture showed twelve colonies of Staph. aureus per plate. Subsequently three more blood cultures were positive. The treatment included rest in bed, local application of ointment and induction of passive hyperemia by constriction of the neck. Bilateral edema of the lids, proptosis and chemosis, dilatation of the retinal veins and impairment of movement of the eyeballs, together with ptosis on the left side, warranted a diagnosis of thrombosis of the cavernous sinus. Without change in therapy, there was gradual improvement, and the patient was discharged as well on Jan. 30, 1922.

Engelhardt [27] regarded recoveries from this disease as curiosities and accidents. He reported a case as follows:

A man aged 41 had a carbuncle of the left ala nasi which lasted for two weeks and was followed, on July 22, 1912, by bilateral proptosis and edema, dilatation of the veins of the eyelids and about both eyes, optic neuritis and a high fever. The right eye was immediately enucleated and the roof of the orbit incised; pus was not found. On July 27 the lower margin of the right orbit was incised, the left ethmoid and sphenoid air cavities were opened and incisions were made on the forehead. On July 28 further incisions were made along venous branches. At no time was pus encountered. The patient improved and was discharged August 24. On September 27 he returned for treatment of purulent otitis media on the left side. In 1914 he had a deep abscess of the thigh. He was seen again in October 1924, at which time the hearing was impaired but the vision normal in the remaining eye. There was no record of blood culture, observation of the ophthalmic veins or examination of the enucleated eye.

Eagleton [28] reported 6 recoveries in cases of his own and referred to various reports previously published. Of recoveries in his own series, the following 3 cases are instances:

One patient had a succession of styes and then, on June 24, received a blow on the right eyelid. On June 28 there was pronounced edema of this eyelid and a temperature of 105 F. On June 29 there were exophthalmos and chemosis. Stock streptococcus antitoxin was administered on this day. On July 2 multiple incisions were made in the orbital tissues without the finding of pus. Injection of the serum was repeated. After a desperate week the patient's condition changed for the better on July 10. The left cornea ulcerated completely. There was fever for sixty days, during which time the left eyeball was enucleated, several metastatic abscesses were incised and a sequestrum was removed from one hand. There was eventual recovery.

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26. Friedmann, M.: Heilversuche bei septischen Allgemeininfektionen, München. med. Wchnschr. **70**:1195-1199 (Sept. 21) 1923.

27. Engelhardt, G.: Zur Pathologie und Heilungsmöglichkeit der nach Gesichtsfurunkel entstandenen und der otogenen Cavernosusthrombose, Arch. f. Ohren-, Nasen- u. Kehlkopfh. **112**:272-285 (Feb.) 1925.

28. Eagleton, W. P.: Cavernous Sinus Thrombophlebitis and Allied Septic and Traumatic Lesions of the Basal Venous Sinuses, New York, The Macmillan Company, 1926; The Carotid Plexus as the Path of Infection in Thrombosis of the Cavernous Sinus, Arch. Surg. **15**:275-287 (Aug.) 1927.

Another patient was a school girl who had a head cold on Oct. 6, 1923, followed by swelling of the left eye on October 10 and of the right eye on October 15. A diagnosis of thrombosis of the cavernous sinus was made on October 16. The temperature was 102.2 F., a blood count showed 25,000 white cells and a blood culture was negative. After ligation of the left common carotid artery and the left internal jugular vein, a large Krönlein flap of the outer orbital wall was reflected and the orbit completely eviscerated. Thick pus was found in the upper part of the orbital cavity. The cavernous sinus was opened. It did not bleed, but no clot was observed. The ethmoid labyrinth was opened from the orbit, and pus was found there. Bacteriologic observations were not recorded. The patient recovered and was discharged October 29.

A third patient had chills and a high fever complicating purulent otitis media and severe tonsillitis. On October 11 the lateral sinus was opened and the internal jugular vein was excised. Several blood cultures were negative. On October 22 there was severe pain behind the right eye and the retinal veins were tortuous, with some hemorrhages in the retina. On this day the right common carotid artery was ligated; the jugular bulb was opened and free pus obtained. Almost at once the temperature fell to normal. The pain behind the eye persisted to a moderate degree for three weeks, but there was eventual recovery.

Eagleton did not give a detailed description of his 3 other recoveries, but he stated that 2 of the patients were treated surgically and 1 recovered spontaneously.

Christophe [29] reported the case of a woman aged 32 who had an infected jaw after repair of a right premolar tooth in October 1926:

In February 1927 she had fever and chills and a rapid diminution of vision in the right eye. On March 8 there was exophthalmos and edema of the lids on the right side, and on March 9 the right eye was fixed, totally blind, painful and full of blood. On March 11, as a measure of desperation, the right common carotid artery was compressed with a small Carrel clamp, over which the cutaneous incision was sutured. Then the lateral wall of the orbit was reflected and the orbital fissure visualized by medial retraction of the orbital tissues. A bit of bone was removed from the lower border of the sphenoid fissure, and the cavernous sinus was easily punctured with a bistoury. Some dark blood escaped, but the clot was not removed. A drain was placed in contact with it and brought out at the inferior external angle of the wound, where it was fixed by a suture. The postoperative condition was satisfactory. Six days later the supraclavicular wound was reopened, the carotid artery ligated and severed and the clamp removed. The orbital drain was removed after fifteen days. The sinus continued to discharge for two months. After complications, including erysipelas about the opening, the patient recovered. On the basis of the erysipelas, the streptococcus was designated as the invasive organism. The author gave credit to Eagleton for the operation and for the successful outcome of the case.

Benjamins [30] observed a boy of 15 who had an exacerbation of otorrhea of three years' standing. Edema of the upper lid, chemosis

29. Christophe, L.: Thrombo-phlébite du sinus caverneux. Opération. Guérison, J. de cir. et ann. Soc. belge de chir. **27**:312-318 (Dec. 29) 1938.

30. Benjamins, C. E.: Ein geheilter Fall von Thrombose des Sinus cavernosus, Monatschr. f. Ohrenh. **65**:1489-1501 (Dec.) 1931.

and proptosis of the right eye occurred after a radical mastoidectomy and incision of an abscess in the neck. The left eye became similarly affected. Both orbits were explored and pus liberated. After incision of various abscesses the patient slowly recovered, with total blindness of the left eye.

Lewis [31] has reported a recovery confirmed by necropsy:

A boy aged 15 had a furuncle near the left angle of the mouth in October 1930. This was incised on two occaasions. He was admitted to the hospital on the fifth day. A blood culture showed Staph. aureus. Bacteriophage was given intravenously, but the details of this treatment were not contained in the published report. The patient was transferred to another hospital on November 18 and first seen by Dr. Lewis on November 21. At this time there were bilateral proptosis and intense chemosis, and a hopeless prognosis was recorded. The neck was stiff, and the spinal fluid contained as many as 1,700 cells per cubic millimeter. Apparently with only expectant treatment the patient began to improve about the middle of December. Mercurochrome, 15 cc. of 1 per cent solution, was given intravenously on Jan. 16, 1931. On April 6 the patient was well except for total blindness of the left eye and various abnormal neurologic signs considered to be evidence of a closed pathologic incident. He resumed school but had an occasional local (staphylococcic ?) infection. On Oct. 13, 1933, without premonitory symptoms he awoke at 4 a. m., vomited several times, became disoriented and stupid; he was removed to the hospital at 7 a. m. and died in a few hours. Necropsy disclosed old fibrinous meningitis and an abscess 24 by 30 by 23 mm. in extent in the right temporal lobe, which had ruptured into the lateral ventricle. There was dense fibrous tissue throughout the left cavernous sinus, in which new blood channels had formed.

Stout [32] used bacteriophage subcutaneously and intrathecally in 2 cases of cavernous sinus thrombosis complicated by staphylococcic meningitis. One patient died within two days, and the observations at necropsy were typical. The other was a girl of 16 who had had a furuncle on her chin:

This appeared July 19, 1930, was lanced four days later and was cauterized on July 25. On July 29 there were exophthalmos and chemosis on the right side and on July 31 an extension to the left eye. A blood culture showed staphylococci. On August 23 the spinal fluid contained 1,100 cells per cubic millimeter, and numerous staphylococci were demonstrated in direct smears and by culture. Bacteriophage was given subcutaneously and intravenously and injected into the spinal canal in doses of 1 to 5 cc. The patient recovered, and on December 1 she weighed 10 pounds (4.5 Kg.) more than she had previous to her illness.

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31. Lewis, E. R.: Cavernous Sinus Thrombosis: Recovery, Ann. Otol., Rhin. & Laryng. **40**:341-347 (June) 1931; Cavernous Sinus Thrombosis—Recovery, Confirmed by Necropsy Three Years Later, Tr. Am. Laryng., Rhin. & Otol. Soc. **40**:378-385, 1934.

32. Stout, B. F.: Septic Cavernous Sinus Thrombosis: Report of Two Cases with Recovery of One Following Bacteriophage Therapy, J. Lab. & Clin. Med. **17**:28-39 (Oct.) 1931.

Turner and Reynolds [1] observed 1 recovery in their series of 21 cases. The patient, a man of 61, had proptosis and chemosis on the right side about two weeks after a mastoidectomy on the left side. Without further operation he recovered, but the blind eye had to be enucleated eventually because of corneal ulceration.

Dupuy, Brewster and Thomas [33] advocated operation on the cavernous sinus before onset of exophthalmos if recovery was to be expected:

Their patient, a 15 year old Negro boy, was admitted to the hospital Feb. 12, 1932 in a stuporous condition, with orbital cellulitis, edema of the lids, exophthalmos and retinal hemorrhages on the left side and a temperature of 102 F. The primary lesion was extensive furunculosis of the upper lip. Four hours after admission the left internal carotid artery was ligated. External canthotomy was followed by enucleation of the left eye. Considerable pus was encountered posterior to Tenon's capsule. The cavernous sinus was entered, the thrombus located and a gauze drain inserted. During the stormy postoperative course four separate blood cultures were positive for Staph. aureus. Improvement followed the intravenous use of gentian violet and mercurochrome. The patient was in good health in May 1932.

Larson [34] described the case of a boy 4 years old:

There was a history of otitis media for four weeks, and a mastoidectomy was performed, with liberation of pus. After a sudden rise in temperature thirteen days later, the mastoid was reopened, but intermittent fever remained and rigors occurred. Edema of the lids, which had been present since admission, subsided, to reappear suddenly associated with chemosis and proptosis. After spontaneous rupture of an abscess through the temporal side of the right orbit on the forty-seventh day there was uninterrupted recovery. Although no bacteriologic studies were recorded antistreptoccus serum was employed in therapy.

Weizenhoffer [35] reported the following case:

A woman aged 29 had cellulitis of the right external auditory canal on March 28, 1931, which continued to spread. On March 31 there was sudden pain in the thorax, with cough and expectoration of blood-tinged sputum. The floor of the auditory canal was incised on April 1, and on this day the temperature rose to 104.6 F. By April 3 the edema had extended to the clavicle. A culture of blood apparently taken at this time showed a growth of Staph. aureus. On April 5 there were proptosis and edema of the left eye, and on April 7 the right eye was swollen shut, the temperature was 105.4 F. and the patient was irrational and incontinent. On April 11 there was evident improvement, the right eye could be opened and the temperature was falling. The subsequent course was stormy, with two serious

33. Dupuy, H.; Brewster, H. F., and Thomas, A.: Left Cavernous Sinus Thrombosis: Case Report, Laryngoscope **42**:931-933 (Dec.) 1932.

34. Larson, B.: Ein Fall von otogener cavernosus Thrombosis mit Heilung nach orbitalen Durchbruch, Ztschr. f. Hals-, Nasen- u. Ohrenh. **30**:663, 1932.

35. Weizenhoffer, A.: Contralateral Cavernous Sinus Thrombosis Following Furuncle of External Auditory Canal: Recovery, New York State J. Med. **32**:139-142 (Feb. 1) 1932.

relapses. Seven transfusions were given from April 11 to May 19. In October 1931 the left external rectus muscle was still weak. The author said that the infection was of low virulence and that the thrombosis evidently extended in a retrograde manner from the jugular bulb along the inferior petrosal sinus.

The case of Browder and Myerson was reported as follows [36]:

The patient, a man aged 23, was admitted to the hospital on April 25, 1932 with a carbuncle on the right side of the nose. A roentgen ray treatment was given on April 26. On April 28 the right eye was swollen and there were slight proptosis, severe headache, slight rigidity of the neck and a temperature of 100.6 F. Culture of blood taken at this time yielded Staph. aureus. Without awaiting more definite developments, the surgeon opened the cranium in the right subtemporal region, retracted the temporal lobe and followed the sphenoid ridge down to the tuberculum sellae. The right cavernous sinus appeared normal. The needle of an electrocoagulating instrument was applied to the wall of the sinus to initiate coagulation and then pushed through into the anterior part of the sinus to accomplish complete obliteration of the lumen. The wound was closed. The angular vein was incised and found to contain creamy pus, from which Staph. aureus was cultured. After the operation there were increasing proptosis and chemosis of the right eye, with absolute fixation of the globe. Orbital pus was evacuated through several local incisions. The right cornea ulcerated, with complete loss of vision in the right eye, forty-eight hours after the operation. On May 11 blood for culture was taken, the first to remain sterile. The patient was discharged sixty-six days after operation. When he was seen a year later, his general condition was good, but the right eye was blind, without reaction to light, and slight ectropion of the lower lid was present.

Claus [37] recommended evisceration of the orbit for prevention of fatal thrombosis of the cavernous sinus. In cases of severe tonsillitis he observed thrombosis of the veins beneath the tonsil, extending to the pterygoid plexus and the temporal region. He noted 5 fatal cases in which the first symptom was a stabbing pain in the eye increased by pressure on the globe. Evisceration of the orbit after edema and proptosis had appeared failed to save the patient's life. However, in a similar case this operation was done as soon as the stabbing pain was recognized and before there were external signs of venous obstruction in the orbit. The patient, a man of 21, was admitted in December 1933 with angina of eight days' standing and a peritonsillar abscess of four days' duration, which had been drained. Then he had a chill, and the characteristic pain in the eye developed. Soon after evisceration of the

36. Browder, E. J.: Carbuncle of Nose: Ophthalmic Vein Phlebitis; Operation for Cavernous Sinus Thrombosis; Recovery; Report of Case, Laryngoscope **43:** 829-830 (Oct.) 1933. Browder, J., and Myerson, M. C.: A Surgical Method for the Prevention of Thrombophlebitis of the Cavernous Sinus, Arch. Otolaryng. **21:** 574-583 (May) 1935.

37. Claus: Exenteratio orbitae bei drohender Thrombose des Sinus cavernosus infolge tonsillogener und dentaler Sepsis, Ztschr. f. Hals-, Nasen- u. Ohrenh. **36:** 315-316, 1934.

orbit, the fever disappeared, and the patient gained 20 pounds (9 Kg.) in a month.

Lauwers'[38] patient was a boy aged 15 who presented the classic picture of thrombosis of the cavernous sinus after several teeth had been removed to relieve severe pain on the left side of the face. At operation the common carotid artery was ligated and the external branch of the inferior ophthalmic vein opened and drained. The presence of a sequestrum retarded complete healing of the wound. Otherwise, recovery was without event.

Gerrie[39] performed a submucous septal resection on a youth of 18 on April 10, 1935. On April 22 there were severe frontal headache, photophobia, rigidity of the neck, a Kernig sign and boggy swelling of the nasal septum, which was again incised. The headache became more severe, and edema and proptosis of the left eye appeared. Later in the day the right eye became involved. The spinal fluid was sterile. Polyvalent streptococcus serum was administered three times and methenamine in doses of 10 grains (0.65 Gm.) every four hours. The patient was discharged May 24.

Cavenagh[40] reviewed several reported recoveries, some of which we have already mentioned, and reported a case of his own:

> The patient, a woman of 26 with chronic otitis media, was admitted to the hospital Nov. 1, 1934 with proptosis and chemosis of the right eye. On November 8 an abscess of the left lateral lobe of the thyroid gland was incised and drained. Subsequently there were severe rigor and a rise in temperature to 104 F. On November 10 the proptosis of the right eye had increased and proptosis of the left eye was recognized. On November 13 the left mastoid was explored and a solid clot was found in the left lateral sinus. The left jugular vein was ligated and an abscess of the anterior cervical triangle drained. There was gradual recovery.

The author stated the belief that this was an example of thrombosis of the cavernous sinus of the chronic compensatory type, probably self limiting and little influenced by the surgical measures.

Jauerneck[41] observed the following case:

> A woman of 34 had an attack of angina which began June 15, 1935 and lasted four days. Her headache persisted and on June 22 the left eye suddenly became proptosed, chemotic and fixed. The right eyelids became swollen on June 23. Operation on this day included eradication of the left ethmoid sinus, through external incision, and deep incision of the left orbit, without the finding of pus in either

38. Lauwers, E.: Deux observations de thrombo-phlébitis du sinus caverneux traiteés par drainage, Bull. et mém. Soc. nat. de chir. **60**:39-43 (Jan. 20) 1934.

39. Gerrie, J.: Cavernous Sinus Thrombosis with Recovery, Brit. M. J. **2**:453 (Sept. 7) 1935.

40. Cavenagh, J. B.: Cavernous Sinus Thrombosis: A Study of the Cases of Recovery, Brit. M. J. **1**:1195-1199 (June 13) 1936.

41. Jauerneck, A.: Geheilte isolierte Kavernosusthrombose wahrschleinlich tonsillogenen Ursprungs, Hals-, Nasen- u. Ohrenarzt **27**:271-273, 1936.

location. Subsequently the right eye became worse, and the right orbit was opened by approach through the maxillary antrum, again without the finding of pus. The patient was discharged after four weeks. Vision in the right eye was somewhat impaired but was found entirely normal after one year. The left eye remained totally blind.

Piquet and Decoulx [42] reported on a patient who had a stormy course following an acute exacerbation of otorrhea on the left side:

Pus was evacuated from the mastoid region, a petromastoid operation was performed and a brain abscess was drained. At the end of five weeks exophthalmos developed in the left eye. About eight days later this became bilateral, and it remained so for a week, when the left eye returned to normal. There was no chemosis at any time. Four months from the onset of the illness, after secondary surgical drainage of the brain abscess, the ocular symptoms had completely disappeared and the patient was considered recovered, although he was still aphasic and had right hemiplegia.

Ledl [43] suggested the use of an antiseptic substance injected into the carotid artery to render sterile the suppurating meninges, the thrombosed cavernous sinus and other gravely infected regions of the head. Rivanol, an acridine dye (2,ethoxy-6,9-diaminoacridinium hydrochloride), was considered by him to have special qualities for this mode of therapy. It was first used in 1923, on a patient in coma with pronounced classic symptoms of thrombosis of the cavernous sinus. The patient regained consciousness but later died. In Ledl's case reported in 1937, the patient was a 32 year old man:

Proptosis and chemosis developed after an attack of angina which occurred at a time when he was about to leave the hospital after a mastoidectomy. The mastoid wound was reopened but appeared healthy. Rivanol was injected by the intracarotid route immediately and continued to be administered almost daily until the temperature became normal and remained so. On removal of the left tonsil during the course of this treatment, it was found to be filled with small abscesses and, on bacteriologic examination, yielded streptococci. The patient made a complete recovery.

MacNeal and Cavallo [44] reported the case of a woman aged 40 in whom there was obstruction of the cavernous sinuses of nasal origin, with all the clinical manifestations of fulminant septic thrombosis, including hemolytic streptococci in cultures of the blood and metastatic pulmonary involvement. Sulfanilamide was administered by mouth and

42. Piquet, J., and Decoulx: Abcès cérébral otitique. Thrombose du sinus caverneux, Guérison, Ann. d'oto-laryng., June 1936, pp. 583-588.

43. Ledl, F.: La thrombophlébite septique du sinus caverneux guérie par des injections du rivanol dans l'artère carotide, Ann. d'oto-laryng., January 1937, pp. 44-49.

44. MacNeal, W. J., and Cavallo, M. E.: Streptococcic Bacteremia and Apparent Thrombosis of the Cavernous Sinuses with Recovery, J. A. M. A. **109**:2139-2141 (Dec. 25) 1937.

streptococcus serum and specific streptococcus bacteriophage intravenously. The patient was discharged after six weeks and has remained free from sequelae in the subsequent four years.

Steinmann [45] called attention to the observation that in many instances of obstruction of the cavernous sinus there is no actually demonstrable thrombus and the obstruction may be explained as due to edema of the structures within the dural sinus. He referred to Bouchet and his associates, who were able to demonstrate on Jan. 18, 1937 an interesting case in which one could follow the development and extension of the lesion, at first an obstruction by pseudothrombotic edema, which might regress, and later a genuine thrombosis of the venous channels within the cavernous sinus. Steinmann reported 2 cases, as follows:

> The first patient, a man of 25, struck his nose with a metal tool in February 1937. The wound healed in eight days, but a month later a furuncle appeared in the scar. On admission of the patient to the hospital, May 3, an incision was made at the point of fluctuation, contrary to the usual practice. The pus yielded staphylococci, and a specific bacteriophage was prepared. On May 4 there was palpebral edema, and on May 5 the right eye was swollen shut, with some proptosis; the temperature was 40.2 C. (104.4 F.) and the condition critical. Dr. Steinmann was familiar with Ledl's intracarotid injection of rivanol and felt that the use of bacteriophage by this route was justified. An intracarotid injection of 3 cc. of bacteriophage was given on this day without a reaction. An intracarotid injection of 20 cc. of bacteriophage was given on May 7 and a third injection, of 20 cc., on May 10. On May 11 the patient was much better, with nasal breathing reestablished and the temperature 38 C. (100.4 F.). He was discharged on June 8, with persistent diplopia due to paresis of the right sixth nerve.
>
> The second patient, a man of 68, was admitted on Jan. 19, 1937 with an old diabetes and bronchopneumonia. As the latter condition improved a furuncle developed at the right wing of the nose, appearing on June 30. An intern, "poorly inspired," incised and curetted this lesion. The culture yielded Staph. aureus and a few streptococci. Soon there appeared chemosis of the conjunctiva. On July 10 an intracarotid injection of 10 cc. of specific bacteriophage was given, and bacteriophage was also administered by mouth. A second intracarotid injection of 10 cc. on July 12 was followed by a slight chill, with a rise in temperature to 39 C. (100.2 F.), and subsequent rapid improvement. A third arterial injection of 10 cc. of bacteriophage was given on July 14. The patient was discharged on August 11.

Goldenburg [46] reported the case of a man aged 22 who observed a pimple on the left side of his face on June 4, 1937:

> This was treated with a 25 per cent erythema dose of radium (gamma radiation) on June 9. The furuncle opened spontaneously, the culture yielding Staphylococcus albus, but frontal headache, several chills and, on June 11, stiffness of the neck and vomiting developed. The patient was admitted to the hospital on this day, at which

45. Steinmann, J.: Injections de bactériophage intra-carotidien pour le traitement des furoncles du nez avec début d'extension vers le sinus caverneux, Schweiz. med. Wchnschr. **67**:1189-1190 (Dec. 11) 1937.

46. Goldenburg, M.: Sulfanilamide in Ophthalmology with Report of a Case, Am. J. Ophth. **21**:54-60 (Jan.) 1938.

time there was cellulitis of the left side of the neck, including the parotid region. The spinal fluid, although under increased pressure, was clear, and a culture was negative. Intramuscular injections of azosulfamide were begun. On June 14 there were pronounced proptosis and mild chemosis of the right eye. The drug therapy was continued. On June 15 a diagnosis of thrombosis of the cavernous sinus was made. The patient recovered and was discharged July 25.

Among the records of the hospitals of Oklahoma City, Wails [47] found 28 cases in which the diagnosis was thrombosis of the cavernous sinus. He described the following case:

A 15 year old girl became ill after squeezing a stye on the left eyelid. Both eyelids were swollen, and there were considerable chemosis of the conjunctiva and marked engorgement of the retinal veins. A blood culture was positive for Staph. aureus. An intensive course of staphylococcus antitoxin therapy was followed by immediate improvement, and it seemed likely that the patient would recover. However, complicating pneumococcic pneumonia was rapidly fatal. No mention was made of autopsy, though the author seemed assured that death was not due to the staphylococcic infection.

Barnshaw [48] reported on a desperately ill patient who responded to expectant treatment:

A 7 year old girl was hospitalized September 20 after having squeezed a stye on the lower left lid three days before. The temperature was 104 F., she was severely toxic and the left eyelid was swollen. There were chemosis of the bulbar conjunctiva and marked proptosis, and the globe was fixed. The right eye was also affected. Staphylococcus was isolated from the blood stream and from the left eye. The child was irrational, with evidence of meningeal irritation. On the thirteenth hospital day a corneal ulcer appeared on the left eye, which perforated but healed quickly. A superficial ulcer of the right eye healed without perforating. Except for impairment of vision, good recovery was achieved, with discharge to the clinic on the fifty-fifth hospital day.

Germán [49] reported 2 recoveries following his operation for removal of the petrous pyramid and excision of part of the wall of the superior petrosal sinus, a procedure recalling that of Bircher (1893). In Germán's cases the infection was due to hemolytic streptococci.

Jeschek [50] in a large series of cases saw only 1 recovery:

A woman aged 43 had a left wisdom tooth extracted three days before admission. Next day there were high fever, edema of the eyelids and nose, proptosis

47. Wails, T. G.: Cavernous Sinus Thrombosis with Case Report, J. Oklahoma M. A. **31**:378-381 (Nov.) 1938.

48. Barnshaw, H. D.: Report of a Case of Bilateral Cavernous Sinus Thrombosis: Recovery Without Operative Intervention, J. M. Soc. New Jersey **36**:22-24 (Jan.) 1939.

49. Germán, T.: Bermerkungen zur Arbeit Dr. Josef Jeschek: "Ueber die Prognose von septischen Thrombosen des Sinus cavernosus," Monatschr. f. Ohrenh. **73**:346 (May) 1939; Ueber chirurgische Behandlung der Kavernosus-Thrombose, ibid. **73**:387-389 (June) 1939.

50. Jeschek, J.: Ueber die Prognose von septischen Thrombosen des Sinus cavernosus, Monatschr. f. Ohrenh. **73**:197-203 (March) 1939.

and chemosis. The temperature at admission was 40 C. (104 F.). A radical operation on the left ethmoid and sphenoid through a supraorbital incision and a puncture of the left antrum were performed. The condition of the eye improved, but two days later there was definite meningitis, with purulent spinal fluid. Methenamine and "prontosil" (preparation not stated) were injected. After nine weeks there was pain in the left hip (metastatic?). This disappeared spontaneously.

The author apparently credited the recovery to the operative procedures rather than to the use of the sulfonamide compound. The bacteriologic findings were not recorded.

Seydell [51] reported the case of a youth aged 19:

There was a severe exacerbation of chronic otitis media on the left side, complicated by bilateral proptosis and chemosis, on Dec. 19, 1938. A culture of material from the ear showed hemolytic streptococci. Sulfanilamide and polyvalent streptococcus serum were given, and there was unexpected, remarkable improvement. On Jan. 3, 1939 a radical mastoidectomy was performed on the left side. A clot was left in the sigmoid sinus, and the jugular vein was not ligated. Nine days later (January 12) there was severe pain in the right eye accompanied by increased proptosis and chemosis. The eyeball was displaced forward and upward. The swelling here was incised on January 27 and considerable pus released. The patient was discharged on February 11. Vision in the right eye was only slightly impaired. The total amount of sulfanilamide given was 144.5 Gm. during thirty-six days.

Morrison and Schindler [52] reported the following case:

A boy of 5 years had a pimple on the left side of the nasal tip on July 21, 1939, which was picked. On July 24 the swelling had extended and the right eye became puffy. On July 27 both eyes were swollen shut, and on July 28 there were bilateral chemosis, a suggestion of stiffness of the neck and a temperature of 104.4 F. Blood for culture taken at this time showed a growth of Staph. aureus on July 29. The spinal fluid was normal. Sulfapyridine (2-[paraaminobenzenesulfonamido]-pyridine) was given, 1 Gm. every four hours, a level in the blood of 10.4 to 16.5 mg. per hundred cubic centimeters being maintained from July 29 to August 6. Then the dose was gradually diminished, and it was finally stopped on August 12. The total amount of sulfapyridine used was 63 Gm. Transfusions and intravenous injections of dextrose solution were also given, to keep the fluid intake between 2,300 and 3,000 cc. daily. The child had made a complete recovery by November 1939.

Lyons [53] recorded 2 consecutive recoveries from staphylococcic thrombosis of the cavernous sinus associated with bacteremia:

A woman of 31 noticed a furuncle of the nose on March 31, 1940 and was treated with sulfanilamide. She was admitted to the hospital on April 5 with

51. Seydell, E. M.: Recovery from Thrombosis of the Cavernous Sinus, Arch. Otolaryng. **30**:429-430 (Sept.) 1939.

52. Morrison, L. F., and Schindler, M.: Cavernous Sinus Thrombosis: Report of a Recovery Following Sulfapyridine Therapy, Arch. Otolaryng. **31**:948-954 (June) 1940.

53. Lyons, C.: The Treatment of Staphylococcal Cavernous Sinus Thrombophlebitis with Heparin and Chemotherapy, Ann. Surg. **113**:113-117 (Jan.) 1941.

edema of the eyelids and the bridge of the nose, unilateral exophthalmos and palpable frontal veins. A blood culture yielded staphylococci, and treatment with heparin and sulfapyridine was started. On April 8 sulfathiazole (2-[paraamino-benzenesulfonamido]-thiazole) was substituted for the sulfapyridine. On April 15 the patient suffered a pulmonary infarction. Use of heparin was discontinued on April 21, after a total of 225,000 units had been given, and administration of sulfathiazole, on April 24. On May 8 there was clinical meningitis and a spinal fluid culture yielded staphylococci. Sulfapyridine therapy was again started. On May 23 the meningitis persisted and sulfathiazole was substituted for the sulfapyridine; its use was continued until October. On June 2 the spinal fluid was normal and the patient was afebrile and symptomatically improved. There were slight residual ptosis of the right upper eyelid and high voltage fast brain waves in the electroencephalogram.

The second patient, a man of 41, was admitted on May 14, 1940 with a furuncle on the nose, edema of the eyelid and the bridge of the nose, exophthalmos, palpable frontal veins, diplopia, ptosis and palsy of the third cranial (oculomotor) nerve and of the first division of the fifth and the sixth nerve. A blood culture was positive for the staphylococcus. Administration of sulfapyridine was started at once and of heparin on May 17. On the next day the patient had a pulmonary infarct. On May 24 sulfathiazole was substituted for the sulfapyridine. On June 1 use of heparin was discontinued, after a total of 580,000 units had been given. The administration of sulfathiazole was continued for three months. There was complete recovery except for residual hyperesthesia of the left frontal region.

Pace [54] reported the case of a boy of 9 years:

The patient was admitted to the hospital on May 29, 1939 with swelling of the face of four days' duration. The right eye was proptosed and immobile, the temperature 103 F. and repeated blood cultures negative. On May 30 the swelling extended to the left side of the face, with proptosis and paralysis of the left eye. Administration of sulfanilamide was started on May 29 in doses of 10 grains (0.65 Gm.) every four hours. On June 1 there was general cyanosis, which was much diminished after administration of methylthionine chloride, 10 grains every three hours for one day. The drug therapy was discontinued on June 13, and the patient was discharged on June 26, entirely recovered. He was quite well seven months later.

Wolfe and Wolfe [55] reported a recovery from thrombosis of the cavernous sinus due to treatment with sulfathiazole:

The patient, a boy 17 years old, pulled a hair from a pimple in his left nostril on Sept. 2, 1940. Four days later there was swelling of the nose and of the left eyelids; sulfanilamide was administered. On September 9 he was admitted to the hospital, semicomatose, with the left eye fixed and chemotic, chemosis of the right eye, edema of the nose and forehead, slight rigidity of the neck and a temperature of 104 F. Through a Levin tube, 2 Gm. of sulfathiazole, together with 1 Gm. of sodium bicarbonate, was given every four hours. This dose of 12 Gm. of sulfathiazole per day was given for fourteen days and then gradually reduced. There was no nausea or vomiting. On September 13 an incision was

54. Pace, E.: Thrombosis of the Cavernous Sinus, Arch. Otolaryng. **33**:216-230 (Feb.) 1941.

55. Wolfe, C. T., and Wolfe, W. C.: Thrombosis of the Cavernous Sinus with Recovery, Arch. Otolaryng. **33**:81-85 (Jan.) 1941.

made near the inner canthus of the right eye, releasing 15.5 cc. of pus. Culture of material from the incision yielded Staph. aureus. Repeated blood cultures were negative. There were a gradual return of function to both eyes and resolution of the edema, until on September 23 motion of the right eye was normal and that of the left only slightly impaired. The patient was discharged on September 30.

Although the diagnosis in this case is open to criticism because of lack of a positive blood culture, of positive evidence in the spinal fluid and lack of postmortem observations, the authors stated the belief that the diagnosis of thrombosis of the cavernous sinus was justified by the evidence.

COMMENT ON RECOVERIES

The preceding list of 58 recoveries is not regarded as complete, and indeed some of the authors quoted have mentioned in their papers recoveries which we have omitted. We have attempted to include those cases in which there was adequate bacteriologic study and others with features of peculiar interest. The diagnosis is open to serious question in some of the cases we have included, for example those of Day (1902), Werner (1905), Coffin (1909), Claus (1934), Jauerneck (1936) and Pace (1941).

The earlier years were dominated by the surgical viewpoint, well expressed in 1918 by Dorland Smith,[56] who emphasized the hopelessness of any measure except surgical intervention. He said, "The process is always fatal if the thrombus is infected and is not drained." At this period there was evidently little if any interest in the bacteriology of the disease. Adair-Dighton used streptococcus serum with success in 1912 in a case of otogenic infection probably due to the streptococcus. Subsequently, streptococcus serum appeared rather prominently in the records of recoveries reported by Eagleton (1926), Larson (1932), Gerrie (1935), MacNeal and Cavallo (1937) and Seydell (1939). In our case (1937) the hemolytic streptococcus was found by blood culture and the serum appeared to be life saving.

The instances of staphylococcic infection are of special interest for our present purpose. We have been able to find 17 cases in which the infection was apparently due to staphylococci. The first 2 cases, those of Chisholm and Watkins (1920) and Friedmann (1923), were well studied. Both patients had positive blood cultures, and both survived with expectant treatment, instituted apparently because any therapeutic effort was considered futile. The infection in Engelhardt's case (1925) started with a carbuncle on the face and was probably due to staphylococci, although bacteriologic studies were omitted. Enucleation of the right eye and multiple incisions about the orbit, into the ethmoid and

56. Smith, D.: Cavernous Sinus Thrombosis, with Notes of Five Cases, Arch. Ophth. **47**:482-496 (Sept.) 1918.

sphenoid sinuses, failed to locate pus. The case reported by Lewis (1931 and 1934) was one of the first in which treatment with bacteriophage was used. Apparently this therapy was held in light esteem and was discontinued too early, so that the patient eventually died because of renewed activity of the infection in temporarily quiescent intracranial foci. Stout (1931) had a most fortunate result in a well studied patient with positive cultures of the blood and of the spinal fluid, treated by bacteriophage given parenterally and by intrathecal injection. Apparently this was the first recorded instance of recovery from staphylococcic septic thrombosis of the cavernous sinus complicated with well established staphylococcic meningitis. Dupuy, Brewster and Thomas cited a case in which there was staphylococcemia with recovery apparently as a result of direct drainage of the cavernous sinus. They emphasized the need for early surgical intervention. Weizenhoffer's patient (1932) had a blood culture positive for Staph. aureus shortly after incision of an infected external auditory canal. The subsequent thrombosis of the cranial blood sinuses evidently extended in a retrograde manner along the inferior petrosal sinus or along the carotid plexus and may possibly have been aseptic. The patient improved with expectant treatment and later received multiple transfusions. A peculiar case was that of Browder and Myerson (1933). These physicians intentionally induced thrombosis of the right cavernous sinus by electrocoagulation, as a prophylactic measure, in a patient with a carbuncle of the nose and extending thrombophlebitis. A culture of blood taken just before the operation showed a growth of staphylococci. The vision of the right eye was sacrificed as a result of the treatment. The operative procedure in this case was rather the converse of the earlier surgical efforts, as it was directed to induce a thrombotic blocking of the cavernous sinus instead of to provide drainage for relieving such obstruction. The principle of prophylaxis was somewhat similar to that of Engelhardt (1925), who sacrificed the eye very early as a measure of life insurance. Steinmann's 2 cases (1937) were evidently instances of a facial furuncle with early obstruction of the cavernous sinus. The response to intracarotid administration of specific bacteriophage was dramatic in both. The infection in Goldenburg's case (1938) started with a facial furuncle from which Staph. albus was isolated in culture. After treatment with radium the inflammation spread. Azosulfamide was given by intramuscular injection. The ocular signs of obstruction of the cavernous sinus appeared rather late, and cultures of blood and of spinal fluid were negative. The importance of antitoxic therapy was pointed out by Wails (1938), when he noted that, despite the presence of staphylococci in the blood stream, toxic manifestations subsided early in the course of therapy with staphylococcus antitoxin.

In the case reported by Barnshaw (1939) recovery occurred with expectant treatment in spite of the presence of staphylococci in the circulating blood and clinical manifestations of meningeal irritation. The laissez-faire policy was considered by this author as the method of choice in such cases. Morrison and Schindler (1940) made a convincing report of successful treatment with sulfapyridine of a boy with entirely acceptable evidence of staphylococcic septic obstruction of the cavernous sinus, including a positive blood culture. Lyons (1941) reported 2 cases of recovery, in both of which blood cultures were positive, there were pulmonary infarcts and treatment was with sulfapyridine, sulfathiazole and heparin. Wolfe and Wolfe (1941) reported success with sulfathiazole in a case in which blood cultures were negative. Undoubtedly we may reasonably expect more reports of the successful use of sulfonamide preparations in the treatment of this disease. Whether the patients treated with these drugs will escape subsequent intracranial sequelae cannot be foretold with confidence.

Thus, of the 17 reported recoveries from staphylococcic septic obstruction of the cavernous sinus, 4 occurred with expectant treatment (1920, 1923, 1932 and 1939), 2 after prophylactic surgical measures (1925 and 1933), 1 after early and radical surgical measures (1932), 4 after bacteriophage therapy (1931, 1931, 1937 and 1937), 1 after antitoxin therapy (1938) and 5 after treatment with sulfonamide compounds (1938, 1940, 1941, 1941 and 1941). It is at least suggestive that the medical measures seem to have a better record than does expectant treatment.

SUMMARY

1. The cavernous sinus is different from the lateral and sigmoid sinuses in that it is more complex, consisting of a maze of venous channels associated intimately with a large arterial vessel, several nerves and an irregular meshwork of fibrillar tissue clothed by endothelium.

2. Obstruction of the cavernous sinus may result from gradual extension of a completely obturating thrombus along a communicating vessel, especially one of the petrosal sinuses, or it may be due to a local edematous swelling of the tissues within the cavernous sinus, followed by formation of a clot, which may eventually disintegrate into pus. The character and the degree of obstruction are as a rule not clearly revealed by the symptoms and signs observable in the living patient.

3. Septic obstruction (obstruction of the sinus due to general marasmus, neoplastic growth and accidental local physical injury are not considered) occurs especially in association with infection of the middle or external ear and most frequently after its operative treatment; with infection of the nose, paranasal air cavities, teeth and jaws, and with abscesses, carbuncles and furuncles about the head or neck. Local

trauma to the primary lesion, whether by the patient, a lay friend or an ill advised physician, plays an important role in the subsequent extension of the infection and the obstruction of the cavernous sinus.

4. The clinical signs and the postmortem changes of thrombosis of the cavernous sinus were first described by Duncan, in 1821. The proptosis and other ocular phenomena were described by Bright in 1831.

5. Reputedly a fatal disease, thrombosis of the cavernous sinus has nevertheless been followed by recovery in many reported cases, in some of which the diagnosis may be accepted without reserve.

6. Bacteriologic diagnosis was lacking in the earlier cases, but in recent years the hemolytic streptococcus and the staphylococcus have been identified as the commonest causative organisms. Patients with the streptococcic form have been treated with success by means of surgical operations, with serum and with sulfonamide compounds.

7. Staphylococcic septic thrombosis of the cavernous sinus has evidently been prevented in some instances by radical prophylactic surgical measures with sacrifice of the eye. After the obstruction has been established, the operative measures seem less likely to be adequate for success. Most recoveries have occurred with expectant treatment, with bacteriophage therapy and with the use of sulfonamide compounds.

303 East Twentieth Street.

CONGENITAL BILATERAL ANOPHTHALMOS VERA WITH UNILATERAL POLYDACTYLY AND CLEFT PALATE

REPORT OF A CASE

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The emphasis here on the term anophthalmos vera is necessary. Difficulty in distinguishing the several similar conditions has led to much confusion in the literature.

It is indeed rare to observe a case of true anophthalmos. Any interference in the growth of an embryo sufficient to produce complete suppression of the front of the forebrain is more likely to terminate development of the embryo; the embryo would be too abnormal to survive.

Allied aberrations which are often confounded with anophthalmos vera are distinguishable embryologically from it. These are congenitally cystic eyeball and microphthalmos.

Anophthalmos vera may be primary or secondary. The primary variety results from a total failure of one or both primary optic vesicles to bud out from the thalamencephalon. No trace of the ectodermal structures of the eye is formed, though there may have been differentiation of mesoderm so that an orbit is present. The autopsies in the cases reported by Recordon and Griffiths [1] and Gallemaerts,[2] in which no trace of the optic nerve, chiasm or tract were found, were substantiating. The secondary (degenerative or consecutive) variety results from atrophy of the optic vesicles, which have formed. The atrophy is believed to be due to some toxic or infectious agent produced within the uterus and introduced through the maternal circulation to that of the embryo. Postmortem examination in the case reported by Heinberg,[3] in which the

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1. Recordon, E., and Griffiths, G. M.: Brit. J. Ophth. **22**:353-360 (June) 1938.
2. Gallemaerts: Ann. d'ocul. **161**:490-496, 1924.
3. Heinberg, C. J.: J. Florida M. A. **12**:253-256 (April) 1926.

optic nerves were present and attached to rudimentary bulbs, pointed in this direction.

Congenitally cystic eyeball results from cessation of development so early that there is a failure of the primary optic vesicle to invaginate successfully, with subsequent cystic dilatation of its cavity. Imperfect differentiation of the neural ectoderm has taken place, and the cavity of the cyst is the cavity of the primary optic vesicle. Instead of an eyeball, the orbit contains a large cyst, in the walls of which are traces of nervous elements, the tissue in the anterior part of the cyst resembling retina and that in the posterior part being pigmented.

Microphthalmos (pseudoanophthalmos) results from arrest of development at a later stage, after invagination of the primary vesicle but before closure of the fetal fissure. A lens vesicle has been formed, and a certain amount of differentiation of the walls of the optic cup is present. The cleft remains open (coloboma of the retina) and the eye is very small. In the microphthalmic eye there is a tendency toward formation of cysts behind and below the eye. Their cavities are in communication with the cavity of the optic cup. Such cysts are distinguished from cysts of the congenitally cystic eyeball by the absence in the latter of microphthalmos. When orbital integument is prolonged and covers the partially developed eyeball, the term cryptophthalmos is applied.

The earlier the disturbance the more marked the anomaly and the more likely the case will be one of anophthalmos vera. While the condition does occur sporadically in otherwise well formed children, more often it is associated with deficient development of the cerebral hemispheres and olfactory lobes and minor abnormalities elsewhere in the body.

Collins and Parsons [4] drew a differentiating line as follows: "When there is a complete failure of the essential nervous mechanism of the eyeball, Anophthalmos is the proper term; when any of the nervous elements are present, no matter how imperfect, Microphthalmos."

Clinically, it is almost impossible to differentiate the varieties of this anomaly. Extreme degrees of microphthalmos are indistinguishable from anophthalmos. In congenital microphthalmos one can sometimes demonstrate at the posterior pole of the orbital fossa elevated black dots surrounded by normal conjunctiva and, perhaps, in addition, bluish black lines 2 or 3 mm. long, radiating out from these dots in an arrangement resembling the pigment arrangement of the iris. These dots represent the undeveloped eyeball. In congenital anophthalmos vera, however,

4. Collins, E. T., and Parsons, J. H., in Posey, W. C., and Spiller, W. G.: The Eye and Nervous System, Philadelphia, J. B. Lippincott Company, 1906, p. 552.

the orbital fossa contains no suggestion of ocular tissue and no remnants of embryonal ocular epiblastic tissue. The ocular muscles and their nerve supply may nevertheless be partly developed. Thorough exploration of the orbital cavities and microscopic examination of any tissue found therein must therefore be undertaken before a case under observation can be properly classified.

REPORT OF CASE

The patient, a girl, was approaching her second birthday when studied by us. The record of her birth revealed that delivery had been spontaneous and without incident; the weight, 6 pounds 1 ounce (2,750 Gm.); the height, 17½ inches (44.5 cm.); the cry, vigorous; the skin, normal, and the temperature, pulse and

The patient, a girl almost 2 years old.

respirations, normal. On the ulnar side of the middle phalanx of the little finger of the left hand there was found a fleshy protuberance resembling a sixth digit. Examination of the mouth revealed complete failure of closure of the soft palate and existence of a wide opening directly into the nasopharynx. The Wassermann reaction of the blood was negative.

The ocular findings were of particular interest. Intact lids were tightly closed. Complete absence of eyeballs was soon noted. The conjunctival sacs appeared to be covered with conjunctiva.

Several months after birth roentgenograms of the skull, spinal column and long bones were all found to be normal. The supernumerary digit was amputated. When the infant cried her eyelids separated and tears "rolled" down her cheeks. At times mucoid secretion was found behind the closed lids. Immediate response to the slightest noise led to the conclusion that the sense of hearing was rather acute.

Examination of the ocular apparatus revealed uniform conditions on the two sides; therefore only one side will be described. The lids were normal and cilia

present. The palpebral fissure from inner to outer canthus measured 1.5 cm. The sac immediately behind the lids was 1 cm. deep, and no tissue resembling any part of an eyeball could be found in this sac. Lacrimal puncta could not be found in either the upper or the lower lid. The orbital margin was well outlined. There was no epicanthus, no entropion and no ankyloblepharon. When the child cried, marked epiphora occurred.

Mentally the child was deficient. A state of deaf-mutism existed. There were four upper central and four lower central teeth. She was not able to stand up unassisted or to walk.

With the child under general anesthesia the lids were retracted. The empty conjunctival sac resembled a socket from which the eye had been enucleated: only the stump of the sutured conjunctiva was missing. The conjunctiva was smooth and continuous in its entirety. The conjunctival sac of each eye, in succession, was incised widely and the orbital cavity diligently explored. No suggestion of ocular tissue in any stage of development could be found anywhere, with the exception of a pinhead-sized nodule in each orbital cavity. These were removed and on microscopic examination proved to be merely lacrimal gland tissue. No blood vessels, nerves or muscles in any state could be found. When a probe was passed into the optic foramens no resistance was encountered; both appeared to be devoid of contents.

The family history was unimportant. The only pertinent facts are that the first child born to the mother was perfectly normal but died of pneumonia at the age of 1 month; that while the mother was pregnant with the patient (the second child) she had nausea and arterial hypertension during the seventh, eighth and ninth months and was admitted with a diagnosis of toxemia of pregnancy, and that a third child—perfectly normal—was born to her after a pregnancy in which there was vomiting during the ninth month but no arterial hypertension.

The causation of this anomaly is not too clear. Both exogenous and endogenous factors must be reckoned with. The former include such hereditary factors as inherent defects of the cell and diseases transmitted from mother to child; the latter, toxemias and intrauterine infections. Experimental conclusions and perusal of the case reports in the literature provide convincing evidence that it is difficult to place responsibility on any specific factor for this embryologic escapade. Besides, one must keep in mind that not all cases of anophthalmos reported are cases of anophthalmos vera. Jess's[5] case, for example, was considered an instance of anophthalmos until discovered to be a case of luxation of the eyeball into the maxillary sinus. Then, again, there have been too few cases in which the orbital contents have been studied microscopically, and too many cases of microphthalmos which have been reported as cases of anophthalmos, for any review figures to be considered as representative of the occurrence of anophthalmos vera. Only investigated cases can be accepted as genuine. It would therefore be far more accurate to consider all groups of case reports as reports of "anophthalmos vera and allied aberrations."

5. Jess, A.: Klin. Monatsbl. f. Augenh. **100**:353-357 (March) 1938.

Experimentally, Ochi [6] injected ether into chick embryos and concluded as follows regarding the histogenesis of ocular abnormalities:

> At the beginning of the development of the embryo, any factor, either chemical or physical, which can disturb the normal condition of the blastoderm itself or its circumference, may bring about an abnormal differentiation of the embryo. If such disturbance of the normal condition is too great, development of the embryo may be entirely arrested. But, if development is still possible, some deformity of the embryo may result, especially teratoma of the head and abnormalities of the eyes, varying according to the degree of disturbance.

He also observed in chicks that the proportion of microphthalmos to anophthalmos was 3:2.

Yudkin [7] found a family of 9 rats (born of normal parents who subsequently were mated anew several times, to produce only healthy stock) who presented anophthalmos and peculiar malformations of the head. Clinical and histopathologic study revealed the eyeballs and the optic nerves and chiasm to be missing. The tissue which ordinarily develops from the mesoblastic layer was present but in an undeveloped form. He concluded that anophthalmos is probably produced by an arrest of growth of the primary optic vesicle resulting from a toxic, infectious or chemical agent introduced from the mother's circulation to that of the embryo in its early stage of development. Stockard [8] and Hoffmann [9] showed that it could be inbred experimentally in laboratory animals.

Some experimental work on vitamin A deficiency performed at the Texas agricultural experimental station is exceedingly interesting. Hale [10] fed pigs on vitamin A–free foods for five months prior to and one month after breeding. All of a litter of 11 pigs were born without eyes. This result led him to the inference that the anomalies were due to a maternal deficiency in vitamin A. It was shown that no primary optic vesicle had budded from the primary encephalic vesicle. In one animal the olfactory nerve also failed to bud from the encephalic vesicle.

Leplat [11] produced this condition in amphibian larvae by introducing toxic substances to interfere with normal development in the very early stages.

Sorsby,[12] in presenting an unpublished manuscript on anophthalmos by James Briggs, one of the growing number of general surgeons at the beginning of the last century who was turning his attention to ophthal-

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6. Ochi, S.: Brit. J. Ophth. **3**:433, 1919.
7. Yudkin, A. M.: Am. J. Ophth. **10**:341-345 (May) 1927.
8. Stockard, C. R.: Anat. Rec. **18**:261, 1920.
9. Hoffmann: Klin. Monatsbl. f. Augenh. **50**:594, 1912.
10. Hale, F.: Am. J. Ophth. **18**:1087-1092 (Dec.) 1935.
11. Leplat, G.: Arch. de biol. **30**:231, 1920; Compt. rend. Assoc. anat. **19**:194, 1922.
12. Sorsby, A.: Brit. J. Ophth. **18**:469-472 (Aug.) 1934.

mology, credited Thomas Bartholin (Amsterdam, 1657) with relating the earliest authentic account of bilateral anophthalmos. The child also presented maldevelopment of the nose and mouth and had six fingers on each hand and six toes on the left foot. Other case reports followed, but it was not until the latter part of the last century that familial cases found their way into the literature. Before Bartholin's case report, Lycosthenes (Basel, 1557) is alleged to have related "a strange medley of fact and fable" of a child lacking eyes and ears but otherwise well formed. Schenk (Frankfort, 1609) noted a similar curiosity. Collins [13] in 1887 cited two instances of multiple cases of bilateral anophthalmos in the same family; in one family two out of three were affected and in the other three out of eight. Mayer [14] in 1888 described a case in which the lacrimal canal and duct were absent. Von Hippel [15] in 1898 collected 86 cases of anophthalmos. The condition was bilateral in 74 per cent and unilateral in 26 per cent.

Our search through the literature since the beginning of this century disclosed 66 case reports (including those of the 33 cases reviewed by MacLean [16]). The condition was bilateral in 72 per cent and unilateral in 28 per cent. Among the patients with the unilateral form, approximately one half showed some developmental defect in the other eye. Six had microphthalmos of the other eye, and Kanda's [17] patient showed, in addition, coloboma of the iris and choroid and persistent pupillary membrane, while Marchesini's [18] patient had only a coloboma of the iris. In Kanda's case the mother had sustained injury to her abdomen during the fourth month of pregnancy. In 5 cases a member of the immediate family or other close relative had a similar condition. McMillan [19] reported 4 cases of anophthalmos and maldevelopment of the eyes in the same family; the patients were children of normal parents. One child had bilateral microphthalmos; 3 had anophthalmos on one side and microphthalmos on the other. Rosenbaum's [20] 2 patients presented a history of consanguinity. With regard to heredity, in Pagliari's [21] case there was a history of chronic alcoholism in the parents, while Rifat's [22] patient had hereditary syphilis of the second generation. A hereditary influence usually shows itself as a recessive malformation.

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13. Collins, E. T.: Roy. London Ophth. Hosp. Rep. **11**:429, 1886-1887.
14. Mayer, M.: Mikrophthalmus mit Cysten im unteren Augenlid, Wurzburg, A. Boegler, 1888.
15. von Hippel, E.: Arch. f. Ophth. **47**:227-241, 1898.
16. MacLean, A. L.: Am. J. Ophth. **12**:381-383 (May) 1929.
17. Kanda, K.: Brit. J. Ophth. **19**:512-519 (Sept.) 1935.
18. Marchesini, E.: Boll. d'ocul. **12**:225-244 (March) 1933.
19. McMillan, L.: Brit. J. Ophth. **5**:121, 1921.
20. Rosenbaum, M.: Congenital Anophthalmos with Orbitopalpebral Cyst, Arch. Ophth. **5**:884-889 (June) 1931; Am. J. Ophth. **19**:1101-1104 (Dec.) 1936.
21. Pagliari, M.: Ginecologia **1**:103-111 (Jan.) 1935.
22. Rifat, A.: Ann. d'ocul. **168**:141-144 (Feb.) 1931.

While speech was usually imperfect and mental deficiency of varying degree the rule, other physical defects were noted in some of the patients. Kanda's [17] patient had atresia elsewhere in the body. Fernando's [23] patient had orbitopalpebral cysts. Rosenbaum's [20] patients both had orbitopalpebral cysts. In one the orbits were slightly undersized. In the other roentgenograms of the head and of the optic foramens showed that the frontal bones were exceedingly rudimentary. The left orbit was slightly smaller than the right; the left optic foramen was much contracted and irregular, and the sella turcica was of infantile type. Grabscheid's [24] patient had no accessory nasal sinuses. Tillim's [25] patient had acute hydramnios and was a hydrocephalic monstrosity.

Few patients have come to autopsy. Recordon and Griffiths [1] found a patent foramen ovale and a teratoma of the brain. They suggested that the latter may have been responsible for the suppression of the optic vesicles. The base of the brain showed complete absence of the chiasm and the optic tracts. The optic foramens were not patent, and the orbits were rather small. However, there was no abnormality of the basal ganglions, their fiber tracts, the internal capsule or the midbrain. Gallemaerts [2] found the skull normal and occipital lobes present. There was no trace of an optic nerve, chiasm or tract. The fourth and sixth nerves were absent. The sella turcica was normal. Orbital muscles were present. No traces of an eye, orbital cyst or rudimentary nodules were found. Heinberg,[3] on the other hand, found optic nerves attached to rudimentary bulbs. Woolard [26] found the optic chiasm and tracts represented by mere threads, but the lateral geniculate body, the superior colliculus and the pulvinar were normal. The third, fourth and sixth nerves were lacking, even though their nuclei were present. Kubick [27] found gross abnormalities of the brain, including a complete lack of the forebrain and the midbrain.

Treatment is sometimes required. Medical care is indicated when the discharge from the conjunctival sac is annoying and causes the lids to adhere. An astringent may be prescribed for use in drops or other form of local application, as in ordinary cases of conjunctivitis, acute, subacute or chronic. Surgical intervention may be indicated for the correction of (1) irritation from in-turning lashes and (2) inability of the conjunctival sac to hold an artificial eye. Prosthesis is necessary and advisable, particularly in cases of unilateral anophthalmos; sometimes it is the ideal means of relief of the first-mentioned condition. Lotin [28] suggested methods of plastic restoration of the conjunctival sac.

23. Fernando, S. E.: J. Ceylon Br. Brit. M. A. **31**:61-63 (June) 1934.
24. Grabscheid, E.: Rev. de laryng. **5**:1184-1189 (Nov.) 1933.
25. Tillim, S. J.: West. J. Surg. **42**:232-234 (April) 1934.
26. Woolard, H.: Brit. J. Ophth. **10**:131-138 (March) 1926.
27. Kubick: Arch. f. Ophth. **112**:234, 1923.
28. Lotin, A. V.: Ruskii opht. J., June 1928, pp. 681-692.

CONCLUSION

Anophthalmos vera is the proper designation only for verified cases. These are distinguishable from instances of similar aberrations by microscopic examination of the orbital contents. Microphthalmos is more common and in cases of unilateral anophthalmos is often found in the second eye. It may be due to recessive hereditary maldevelopment or to an antenatal inflammatory process or toxic factor. It has been produced experimentally in laboratory animals. Autopsy usually reveals anomalies of the central nervous system.

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ROLE OF THE MEDICAL SOCIAL WORKER IN AN OPHTHALMOLOGIC SERVICE

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Before the service of a medical social worker especially trained for work with patients in an ophthalmologic service was initiated in the Hospital of the University of Pennsylvania, it was decided to survey the patient group for the preceding year in order to determine what kinds of patients needed social care and how the worker could best concentrate her efforts to benefit the patients and the service. This was deemed desirable because numerous studies have shown much waste of the ophthalmologist's time in the clinic through the patient's lack of understanding of his ophthalmic conditions and, therefore, a failure to carry out the plan of treatment recommended.

During the year 1940, 1,636 new patients came to the ophthalmologic clinic of the University Hospital. Of these every third patient was chosen for the study, making a total of 599. A large sample was taken in this way because it would cover the complete clinic year, so that no allowance had to be made for seasonal variations, and because it formed a group large enough to make statistical analysis valid. Each chart was reviewed and the following information tabulated: (*a*) identifying social data—sex, race, residence, age, occupation and financial status, and (*b*) some medical facts—previous treatment, whether the patient was known to other clinics in the hospital, number of clinic visits and hospitalizations and status of treatment.

The diagnostic grouping was done with emphasis on etiologic factors. The classification was similar to the one used in the "Classification of

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The survey here reported was made with the help of the staff of the National Society for the Prevention of Blindness. Detailed charts and a full discussion of diagnostic groupings are available in the Social Service Department of the Hospital of the University of Pennsylvania and in the office of the National Society for the Prevention of Blindness.

At the request of Dr. Francis H. Adler, chief of the Department of Ophthalmology, Hospital of the University of Pennsylvania, the National Society for the Prevention of Blindness and the Social Service Department of the hospital cooperated in placing a medical social worker in the ophthalmologic service.

1. Derby, G. S.: The Need of Medical Social Service in Eye Clinics, J. A. M. A. **98**:394 (Jan. 30) 1932. Ross, F.: A Medical Social Study of Patients Who Have Primary Glaucoma Treated at the University of Chicago Clinic, January, 1937 to January, 1940, unpublished data.

Causes of Blindness" developed by the Committee on Statistics of the Blind and used as a standard classification by the Social Security Board.[2] An adaptation of this classification had to be made to include patients attending the clinic but not blind.

Certain general characteristics of the 599 patients are summarized in table 1.

The age groups cover a wide range but roughly divide the patients into those below earning age, those of earning age and those above it, the largest single group, 19 per cent, being between the ages of 20 and 29. The clinic primarily serves an adult group, as 80 per cent of the patients were over 20 years of age. The largest number of patients, 67 per cent, were between the ages of 20 and 60. This is the normal earning period of life, in which good eyesight is of great economic importance.

TABLE 1.—*Status of Treatment and Age, Sex, Race, Fee and Occupation*

	Age			Sex		Race		Clinic Fee		Occupation	
Status of Treatment	Under 20	20-59	60 and Over	Male	Female	White	Negro	Paid	Ad-justed*	Em-ployed	Unem-ployed
Complete, 313.....	53	221	39	134	179	259	54	153	160	101	212
Incomplete, 286.....	69	183	34	133	153	225	61	132	154	80	206
Total, 599.....	122	404	73	267	332	484	115	285	314	181	418

* In this column are grouped patients who could not afford to pay the regular clinic fee and for whom adjustments had to be made for a reduced fee or no fee.

Sixty-eight per cent, a little over half of the patients, were housewives, students or unemployed persons. Of this number, 49 per cent failed to complete recommended treatment. Thirty-two per cent of the patients were employed, and 44 per cent of these failed to complete recommended treatment. These figures are striking, since they show that there is little relation between the patient's employment and his ability or willingness to carry out treatment. The occupational groups with the highest percentage of completed treatment were the salesmen and those in professional services. It is of serious concern to find a large percentage of failure to complete treatment among skilled workers, factory operators, office workers and students.

It appears from the findings that whether or not a patient is charged a fee has little relation to his ability to carry out recommended treatment. Nor is this ability related to distance from the hospital, for the majority of patients registering at the University Hospital live in the city of Philadelphia or its immediate environs. Only 5 patients resided outside the state.

2. Standard Classification of Causes of Blindness, United States Federal Security Agency, Social Security Board, 1940.

Although the majority of patients known to the clinic were adults, 44 per cent had had no previous ocular complaint. Only 3 per cent of the total group, 22 patients, had received treatment from private ophthalmologists or physicians, while 26 per cent, or 155, were wearing lenses prescribed by optometrists. Forty-three of the patients, 7 per cent, had had service at other clinics or hospitals, and 64, 16 per cent, were wearing glasses or had had service from unknown sources.

Practically half of the patients were known to be attending other clinics in the hospital. The majority of these patients were known to the medical service; the second largest number, to the neurologic service. When there was a definite connection between the ocular condition and the physical findings of another clinic, a complete résumé of these findings was incorporated in the ophthalmic record.

The number of clinic visits made by the 599 patients varied from none to over twenty. The patients who made no visits to the clinic were 14 who had been admitted directly to the ward and failed to come to clinic for follow-up treatment after discharge, as recommended on the chart. Twenty-six per cent made only one visit to the clinic. Some of these patients were recorded as having no ocular disease, and a return visit was not indicated. Of the patients, 238, or 40 per cent, made only two visits to the clinic. Of this number, 103 patients had refractive errors, and the physicians of this clinic consider two visits sufficient for completion of treatment.

Eighty-eight periods of hospitalization were given to 64 patients, or 11 per cent of the total of 599. The periods varied from two days to over thirty days, the average length of stay being four days.

The purpose of every ophthalmic clinic is to diagnose, treat and relieve the patient's condition. This particular clinic has other functions —namely, the teaching of both medical students and graduate physicians in ophthalmologic diagnosis, treatment and clinical research. The patient's return to the clinic is essential for the fulfilment of these purposes.

Two important factors in ophthalmic care are skilled service and the ability of the patient to utilize that service. In this survey special consideration was given to the patients' apparent ability to use the available skilled services to the best advantage, and ways in which a medical social worker might have helped them will be pointed out. Of the 599 patients studied, 52 per cent completed treatment and 48 per cent failed to carry out prescribed treatment. The relation of the condition found and the completion of treatment is shown on table 2.

A large majority of the patients in whom the underlying cause of the ocular complaint was syphilis failed to carry out the recommendations made. Since all these patients had information about their general

physical condition, it seems fair to assume that they did not understand or appreciate the grave danger of syphilis to vision.

Many patients are confused and worried at the time of their examination and do not grasp the full meaning of the physician's recommenda-

TABLE 2.—*Relation of Condition Found to Completion of Treatment*

Diagnoses	Total Patients	Completed Treatment	Did Not Complete Treatment	Attended Other Clinics	Hospitalized	Received Previous Medical Attention Related to Eye
Total	599	313	286	330	88	607
A. Infectious diseases						
1. Syphilis	12	2	10	15	2	12
2. Other	6	1	5	8	7	6
B. Trauma						
1. Injuries by foreign bodies	9	7	2	..	1	9
2. Penetrating injuries	3	2	1	..	3	3
3. Burns	6	4	2	1	2	6
4. Other	5	4	1	1	2	5
C. General diseases						
1. Diabetes	9	4	5	11	1	9
2. Vascular diseases	90	43	47	73	..	93
3. Diseases of central nervous system	11	6	5	8	2	12
4. Other	8	1	7	9	2	8
D. Neoplasms	7	6	1	12	4	7
E. Diseases of prenatal origin						
1. Congenital cataract	2	2	..	1	..	2
2. Other	3	1	2	2	1	3
F. Diseases with cause unknown to science						
1. Glaucoma	10	3	7	3	10	10
2. Senile cataract	14	7	7	5	3	15
3. Strabismus	36	17	19	17	4	36
4. Myopia	25	18	7	7	..	26
5. Other refractive errors	191	110	81	72	1	193
6. Other	3	1	2	1	..	3
G. Diseases with other causes unknown						
1. Optic nerve atrophy	9	4	5	7	1	9
2. Diseases of retina	5	2	3	2	1	5
3. Diseases of uveal tract	9	4	5	7	7	9
4. Diseases of cornea	20	9	11	11	4	21
5. Diseases of conjunctiva	30	15	15	7	..	30
6. Diseases of lids	29	15	14	8	5	29
7. Other diagnosed ocular conditions	2	1	1	1	1	2
8. Diagnosis not completed	16	1	15	14	2	16
H. No ocular disease	29	23	6	27	2	29

tion. A second, unhurried interview with a social worker in a quiet office affords an opportunity for the patient to ask questions, to express his fears and to discuss his problems frankly.

It appeared that the important recommendation made in the ophthalmologic clinic to all patients grouped as having "general diseases" was treatment of the particular systemic disease. It was with relation

to such treatment that the social worker could be of assistance by interpreting the relation between general illness and ocular symptoms. The physician can give medication and instructions in proper living and diet, but it is important to know whether or not the patient understands and is able to follow instructions. The removal of social obstacles to assure complete treatment is the responsibility of the medical social worker.

Many of the patients suffering from glaucoma become discouraged with the long period of treatment.[3] The medical social worker has a definite role in the care and treatment of such patients, as a great deal of interpretation and of modification of the environment are needed. The necessity for recommended surgical intervention must be explained; the patient must be encouraged to check up on his physical condition by periodic medical examinations. Many ophthalmologists stress the importance of good hygiene and of the patient's being free from worry as absolutely necessary to successful treatment. Frequently the patient with glaucoma is forced to give up his occupation or profession and seek one that requires less acute vision. Such a step is difficult, and often the patient needs help in making the adjustment. The social worker's role is in helping to modify the attitude of both the patient and his family and in helping the patient understand and accept what the physician has recommended.

COMMENT

Among the 599 patients whose cases were reviewed, some were found who were evidently able to accept the procedures necessary for complete medical study and treatment. Others, almost one half, suffering from a wide range of ocular complaints, did not profit fully from the services offered by the clinic. The reasons for these patients' failing to complete treatment are not evident from the medical charts. However, previous knowledge of patients with ophthalmic complaints and their reactions suggests some of the difficulties they faced.

It is important to know what the handicap means to the patient and to help him to adjust to it or to the treatment necessary to remove it. In children who have ocular handicaps often peculiar behavior develops. Wearing glasses makes one different and often the victim of ridicule. The myopic child is not able to compete in sports; he may, therefore, become retiring. The hyperopic child sees well only at a distance and therefore becomes bored with school work and often becomes a problem in the classroom. The cross-eyed child is more frequently ridiculed and may become retiring and refuse to join other children. Interpreting the child's handicap to both the parents and the school is the function of the social worker. When sight-saving class education is advised by the

3. Gradle, H. S., and Jensen, A. F.: The Need for Social Service Work in Glaucoma, Am. J. Ophth. **22**:993-995 (Sept.) 1939.

physician, the social worker is able to interpret this to the parents so that the aims of the class will be carried out in the home.

Usually patients whose ocular complaints are of prenatal origin are very young, which necessitates interpretation of findings to the parents. Parents are slow to recognize and accept handicaps in their children, and many labor under the illusion that the condition will clear when the child grows up. The patients are often handicapped throughout life, and only certain types of employment are possible for them.

Emotions often shown by young adults who come to the ophthalmologic clinic are fear and resentment. Ocular difficulties during the employable years are a threat to economic security and also to the patient's position in the family and in society. The medical social worker may assist the young patient to accept the treatment plan by allowing him to talk out his fears and inhibitions. When a young adult is experiencing a loss of vision, plans for vocational rehabilitation should be considered. A social worker has much to offer such patients in removing antipathy to treatment and in planning rehabilitation.

Diminishing eyesight in old age increases the already present feelings of insecurity and inadequacy. The reality of an ocular diagnosis is often avoided because it is unpleasant. Elderly persons often become discouraged by the length of medical treatment, expect a miraculous cure and are disappointed when they do not get it. Meeting such patients where they are, both emotionally and intellectually, and proceeding with them through the period of adjustment to treatment is one of the most important contributions of a medical social worker.

Most human beings are afraid of surgical procedures. They rarely will express this fear to the physician. They may become inarticulate and frightened. They cannot help the physician, and the busy physician cannot freely help them. In this situation the social worker can help both the physician and the patient. A patient is better able to adjust to his handicap when medical care and treatment have been geared to meet the social and emotional problems involved.

SUMMARY AND RECOMMENDATIONS

The main purpose in making this survey was to attempt to determine through a study of the patient group where the social worker should concentrate her efforts in order to give the best service to the patient and to the physician and to contribute to the general conservation of vision. A medical social worker's largest contribution to any medical service is her ability, by reason of her training, to understand the meaning of illness to the patient and to help him to meet the emotional and social problems arising from and related to his illness.

Because social and emotional problems keep many patients from completing treatment, an ophthalmologic service must have a trained medical social worker to meet these problems, giving help to the patients and preventing the waste of ophthalmologic service.

Although only 2 per cent of the group studied actually refused the medical recommendations, 48 per cent failed to carry out prescribed treatment. It appeared that employment and ability to pay a clinic fee had little effect on completion of treatment.

From previous experience with patients with ocular disease, it is assumed that the patient's fear of surgical intervention and lack of understanding of the condition, its implications and the treatment planned and of how to make the adjustments necessary to carry it out are among the most common reasons for lack of completion of the treatment recommended.

It is suggested that the following patients be referred by the physician to the social worker for social study and planning:

A. All patients whose social problems appear to be obstacles to prescribed medical treatment and recovery.

B. All patients with certain diagnoses considered especially hazardous to vision, such as keratitis, iritis, glaucoma, cataract, progressive myopia, strabismus, optic neuritis, retrobulbar neuritis and tuberculous lesions.

C. All patients who refuse suggestions for surgical intervention or hospitalization.

D. All children referred for special educational plans.

E. All patients for whom lenses are prescribed which cannot be procured through regular channels.

The social worker should incorporate in the medical chart a summary of the social findings, giving factors in the social situation which relate to the medical picture.

It is necessary for the social worker to have an office in the clinic setting where she will be readily available to both the physician and the patient. The patients see her then as a part of the whole service, designed to meet their needs. She is available to the physician, who may wish to discuss individual cases with her.

It is also advisable for the worker to accompany physicians on regular ward rounds. This is the best way for her to increase her own medical knowledge and to keep in touch with the patient's changing medical situation. The patient sees the worker as a part of the treatment group and will be more likely to recognize the place of her services in the medical plan.

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THE p_H AND TONICITY OF OPHTHALMIC SOLUTIONS

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The hydrogen ion concentration of the solution in which an ophthalmic drug is dissolved may alter the therapeutic results of the drug itself. A variation of the p_H often determines the speed and the quantity of absorption of the drug and the amount of irritation which the patient experiences on instillation.

However, not only the p_H but the osmotic pressure of the resultant solution is important. The lacrimal fluid is alkaline, with a p_H of 7.4, and is isotonic with a 1.4 per cent solution of sodium chloride. This means that the two fluids have the same osmotic pressure and in this instance the same freezing point, at 0.9 C. A hypotonic solution will cause passage of fluid into the ocular tissues, bringing about congestion in an attempt to reach an osmotic balance. A hypertonic solution, on the other hand, will cause the removal from the tissues of fluids which flow in the direction of the solution. Both of these solutions cause irritation, discomfort and excessive lacrimation, while an isotonic solution, such as 1.4 per cent sodium chloride, may be used without sensation or irritation.

Physiologic solution of sodium chloride at a p_H of 7 to 8 causes no sensation, but with a p_H of 9 on the alkaline side some irritation is experienced. As one approaches the acid side, a p_H of 6.3 to 6.6 will result in a dry feeling, and as the solution becomes more acid, that is at a p_H of 4.5 to 6, the patient often experiences considerable discomfort and burning.

Thus it may be seen that the solution in which the drug is dissolved should, if possible, approximate both the p_H 7.4 of tears and the osmotic pressure of the lacrimal fluid in order that the optimum absorption and therapeutic action of the drug and the minimum discomfort to the patient may result. The range of comfort varies approximately from p_H 6.5 to p_H 7.8.

Sometimes an approach to this range is not possible, because of the physical properties of certain drugs, which are soluble only within certain limits of reaction. For example, Lipshütz [1] stated that zinc salts are precipitated and made inactive in an alkaline solution and must be used in an acid solution with a p_H of 5.5 to 6 to produce

1. Lipshütz, H.: Ueber die Bedeutung der Wasserstoffionenkonzentration im Bindehautsack, Klin. Monatsbl. f. Augenh. **82**:763, 1939.

the best therapeutic effect on the conjunctiva. However, Arrigoni, Fischer and Tozer [2] adjusted the p_H of a zinc sulfate solution to 6.75 and made it isotonic with the lacrimal fluid. They used an alkaline solution containing sodium acetate and zinc sulfate and an acid solution of boric acid and zinc sulfate. Potassium chloride was added to each of these solutions until they were isotonic with the lacrimal fluid. Then, in order to obtain the final p_H of 6.75, the two solutions were mixed in the required proportions. The resulting solution, obeying the laws of tonicity and p_H, was not irritating to the eye.

Butyn sulfate, epinephrine hydrochloride and cocaine hydrochloride are precipitated in salt solutions with less than a p_H of 5.9 but are soluble in distilled water, while phenacaine hydrochloride is soluble only in solutions as acid as p_H 5.8.

Gifford and Smith [3] found that some of the common metal salts and alkaloids used in ophthalmology when dissolved in distilled water have the following p_H:

1 per cent atropine sulfate	5.8
2 per cent homatropine hydrobromide	5.5
2 per cent cocaine hydrochloride	4.6
1 per cent pilocarpine nitrate	4.8
0.2 per cent physostigmine sulfate	6.6
4 per cent procaine hydrochloride	4.6
2 per cent butyn sulfate	5.4
0.9 per cent sodium chloride	7.0
0.2 per cent zinc chloride	5.0
Boric acid, saturated solution	4.2

These drugs when used in a saturated solution of boric acid showed reactions varying from p_H 4.2 to p_H 5.

In order to obtain the desired p_H for ophthalmic solutions Gifford [4] used a standard acid buffer solution (solution 1) and a standard alkaline solution containing anhydrous sodium carbonate. When the two solutions are mixed in the required proportions, a final solution with the desired p_H is obtained, as illustrated in the accompanying table. The Gifford method may be used to obtain the desired p_H.

For butyn sulfate and phenacaine hydrochloride, acid buffer solution 1 with a p_H of 5 is used.

The zinc salts, cocaine hydrochloride and epinephrine hydrochloride are dissolved in acid buffer solution 2 with a p_H of 6, which is prepared by adding 0.05 cc. of the standard alkaline solution to 30 cc. of the standard acid solution.

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2. Arrigoni, L.; Fischer, L., and Tozer, G. A.: Ophthalmic Zinc Sulphate Solution, Arch. Ophth. **26**:852 (Nov.) 1941.

3. Gifford, S. R., and Smith, R. D.: Effect of Reactions in Ophthalmic Solutions, Arch. Ophth. **9**:227 (Feb.) 1933.

4. Gifford, S. R.: Relation of Buffer Solutions and Ophthalmic Drugs, Arch. Ophth. **13**:78 (Jan.) 1935.

For the salts of most of the alkaloids, such as atropine, homatropine, scopolamine, pilocarpine and physostigmine, alkaline buffer solution 1 with a p_H of 7.6 is best. This is prepared by adding 1.5 cc. of standard alkaline solution to 30 cc. of Gifford's standard acid solution. These alkaloids are less irritating, are absorbed more quickly and are transmitted in greater quantities through the cornea in this solution than in a saturated solution of boric acid or in distilled water. In spite of the common belief a solution of physostigmine salicylate which turns pink in this medium is not impaired and may be used safely and effectively.

Gifford's System for Obtaining Desired p_H of Ophthalmic Solutions

Gifford standard acid solution:	Boric acid	12.4 Gm.
	Potassium chloride	7.4 Gm.
	Distilled water	1,000.0 cc.
Gifford standard alkaline solution:	Sodium carbonate, anhydrous	21.2 Gm.
	Distilled water	1,000.0 cc.

p_H	Gifford Standard Acid Solution, Cc.		Gifford Standard Alkaline Solution, Cc.	Special Designation
5.0	30.0	plus	0.00	Acid buffer solution 1
6.0	30.0	plus	0.05	Acid buffer solution 2
6.2	30.0	plus	0.10	
6.4	30.0	plus	0.15	
6.6	30.0	plus	0.20	
6.8	30.0	plus	0.30	
7.0	30.0	plus	0.60	
7.2	30.0	plus	1.00	
7.4	30.0	plus	1.25	Normal lacrimal fluid
7.6	30.0	plus	1.50	Alkaline buffer solution 1
7.8	30.0	plus	2.00	
8.0	30.0	plus	2.50	
8.2	30.0	plus	3.00	
8.4	30.0	plus	4.00	Alkaline buffer solution 2

Fischer [5] (1931) presented the following tabulation to illustrate the effect of the p_H of a solution on the absorption of the alkaloids:

	p_H	Concentration in Aqueous, Percentage
1 per cent atropine sulfate	4.0	0.01
	7.5	0.03
	11.0	0.036
0.5 per cent scopolamine sulfate	4.0	0.01
	7.5	0.01
	11.0	0.03
0.5 per cent physostigmine sulfate	4.0	0.015
	7.5	0.025
	11.0	0.03
0.5 per cent pilocarpine sulfate	4.0	0.020
	7.5	0.01
	11.0	0.01

5. Fischer, F. P.: Ueber die Durchlässigkeit der Hornhaut für Alkoloide, Arch. f. Augenh. **104**:121, 1931.

One sees from this table that the absorption into the aqueous chamber of a 1 per cent solution of atropine sulfate is three times as great when the p_H is increased from the acid side of 4.0 to the alkaline side of 7.5, which is that of the lacrimal fluid. The amount of absorption of 0.5 per cent scopolamine sulfate is not affected by a change from p_H 4.0 to p_H 7.5 but is increased three times when the alkalinity is increased to p_H 11.

With a solution of 0.5 per cent physostigmine sulfate the amount of absorption is increased one and two-thirds times when a change from a p_H of 4.0 to a p_H of 7.5 is made. On the other hand, with 0.5 per cent of pilocarpine sulfate solution an increase in alkalinity from 4.0 to 7.5 causes a decrease of about one half in the amount of absorption of the drug into the anterior chamber.

Regnier discovered that when he increased the p_H of a 1 per cent solution of cocaine hydrochloride toward the alkaline side, there was a decided acceleration of its passage through the cornea into the anterior chamber and that its anesthetic properties were decidedly improved. When the p_H of this solution was increased from 3.2 to 8.7, there was a sevenfold increase in its rate of absorption, with resultant improvement of its anesthetic potency. With a p_H of 3.2 it required twenty to thirty minutes to produce complete anesthesia, while only two to five minutes was required when the p_H was increased to 8.7. A 1 per cent solution with a p_H over 7 is more quickly and completely absorbed by the cornea.

The following list shows the concentration of solutions isotonic with lacrimal fluid (expressed in gram per hundred cubic centimeters of solution of aqueous):

Alum (ammonium)	7.8	Pilocarpine hydrochloride	7.0
Atropine sulfate	15.0	Pontocaine hydrochloride	8.2
Borax	4.5	Potassium chloride	1.8
Boric Acid	3.1	Potassium nitrate	2.4
Chlorobutanol	7.6	Potassium sulfate	3.3
Cocaine hydrochloride	9.8	Procaine hydrochloride	7.5
Copper sulfate	11.0	Scopolamine hydrobromide	12.6
Dextrose	7.5	Silver nitrate	4.0
Emetine hydrochloride	12.0	Silver, mild protein	45.0
Ephedrine hydrochloride	5.8	Sodium benzoate	2.8
Ephedrine sulfate	9.2	Sodium bicarbonate	2.0
Ethylmorphine hydrochloride	11.0	Sodium biphosphate	4.0
Homatropine hydrochloride	10.2	Sodium chloride	1.4
Lactose	14.0	Sodium nitrate	2.0
Metycaine hydrochloride	8.2	Sodium sulfate	6.0
Morphine hydrochloride	10.8	Sucrose	15.0
Morphine sulfate	16.3	Tannic acid	13.9
Phenacaine hydrochloride	9.7	Tutocaine hydrochloride	8.6
Physostigmine salicylate	17.8	Zinc sulfate	8.2
Phenol	4.3		

This tabulation is used in the following manner: Suppose one wishes to determine what quantity of potassium nitrate should be added to 100 cc. of a 1 per cent solution of silver nitrate to make it isotonic with the lacrimal fluid.

Step 1: Determine the percentage of isotonicity of the unadjusted solution (refer to silver nitrate in the table: $\frac{1}{4} \times 100 = 25$ per cent isotonicity).

Step 2: Determine the percentage of isotonicity to be supplied by the isotonic agent (subtract the first result from 100: $100 - 25 = 75$ per cent).

Step 3: Compute the weight of the isotonic agent needed (refer to potassium nitrate in the table: 2.4 Gm. $\times$ 0.75 = 1.8 Gm.).

Therefore 1.8 Gm. of potassium nitrate should be added to every hundred cubic centimeters of 1 per cent solution of silver nitrate to make it isotonic with lacrimal fluid.

Colorimetric methods are sometimes used to determine the p_H of a small quantity of a given fluid quickly. The indicators used are as follows:

p_H Indicator	p_H Range	Color Reaction
Methyl red	4.2-6.2	red-yellow
Bromthymol blue	6.0-7.6	yellow-blue
Phenol red	6.8-8.4	yellow-red
Thymol blue	8.0-9.6	yellow-blue

The colorimetric determination of the p_H of a solution consists of comparing the color with that of a suitable buffer solution after the addition of the same quantity of indicator.

SUMMARY

The p_H and the tonicity of an ophthalmic solution determine the rate and the amount of absorption of the drug and its therapeutic action.

The closer the approximation to p_H 7.4 and the tonicity of the lacrimal fluid the less the irritation, discomfort and lacrimation experienced by the patient.

How to determine the desired p_H and tonicity of a solution is illustrated.

55 Eastern Parkway.

KODACOLOR FUNDUS PRINTS

A NEW TECHNIC

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NEW YORK

The Eastman Kodak Company has placed a new color film on the market—Kodacolor roll film. This film differs from Kodachrome film in that it is available in roll film sizes from "vest pocket" to postcard size and the end result is not a transparency but a color print. Kodacolor film is designed for making snapshots in sunlight. Nevertheless, it finds certain applications under which it can be exposed to artificial light. The film, properly exposed, is processed at Rochester, N. Y., and the negatives are returned as color negatives; that is, the colors are reversed. Reds are represented as cyan (blue-green) dye images, greens are magenta and blues are developed as yellow. The negatives are then printed (at Rochester) by projection—the resultant print being a sparkling full natural color print with colors normal in appearance. This process makes the best type of color print available in the lower price brackets, and the expense is considerably less than that entailed in earlier methods.

It is to be noted that the new Kodacolor process has nothing in common with the now obsolete Kodacolor process for 16 mm. motion pictures, which the Eastman Kodak Company introduced a number of years ago and which was superseded by the Kodachrome process.

The great majority of fundus photographs are taken on the Zeiss-Nordenson camera, a special roll film adapter being used, with regular Kodachrome or Kodachrome type A films (Bantam type), eight exposures to a roll of film. The processed film is returned as transparencies suitable for 2 by 2 inch (5 cm.) lantern slides. The picture must be viewed against a bright light source or be projected, and it is the only copy of the exposure unless a duplicate transparency is made by the Eastman Kodak Company or a print is made by the kodak Minicolor process. A print by this process, while excellent, costs almost twice as much as a Kodacolor print. Black and white copies of the Kodachrome transparency require an intermediate black and white negative before a final print is possible. The Kodachrome method is excellent when slides for teaching are desired, but not entirely satisfactory for keeping records or sending copies to colleagues, except when the somewhat more expensive Minicolor prints are made.

It occurred to me that one could employ Kodacolor film easily in fundus photography by merely using the 127 roll in the adapter and

using the arc light, which approximates daylight in quality of color. (The adapter is actually made to fit the 127 film, and special reducing ends must be applied to make the bantam film fit.) The technic involved the putting of the film in the adapter without the reducing ends. The film was wound to the I marking on the indicator. The rheostat power was reduced one third of the way from its present setting, for Kodacolor film is faster (Weston 20) than Kodachrome film type A (Weston 12). The exposure was made in the usual manner, the film turned to the 2 marking for the second exposure and the roll finished at the 6 marking. Extreme care has to be taken in exposing the film according to the numbers marked on it, for the Eastman Kodak Company requires an unexposed end portion in their processing. The roll after exposure should be sent to Rochester, N. Y., for processing.

The resulting prints are excellent. The fundus picture as a print is 2½ inches (6 cm.) in diameter and compares well with a painting, having the advantage of being a fairly accurate color image. The negatives are in the former size, 1¼ inches (3 cm.) in diameter, and any number of prints may be made from each negative, in black and white as well as in color. The cost, including negative, processing and print, is about 58 cents per print, truly a small price for these beautiful pictures. Duplicate prints are priced at 40 cents each.

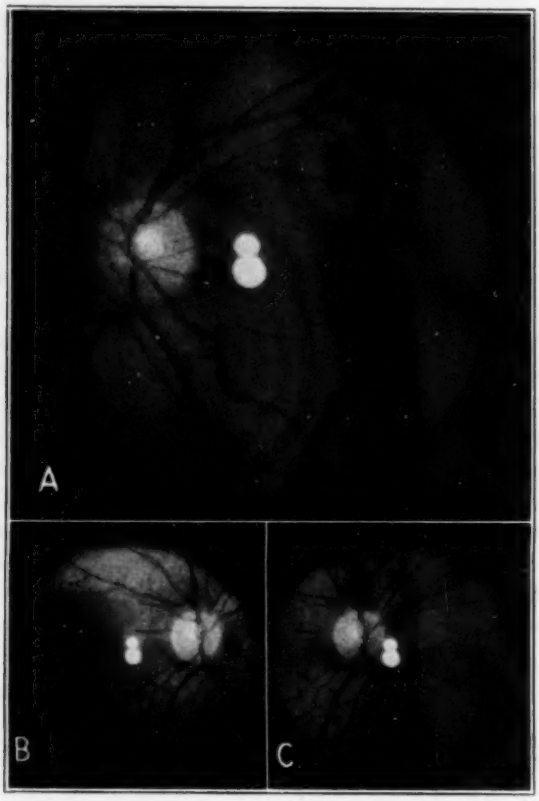
The introduction of Kodacolor film, and its adaptability to the fundus camera, mark a decided advance in ophthalmic photography. Records of fundus lesions in full color may be placed with one's own office records or sent to colleagues. The prints occupy little space and tell much more than the usual sketch of a given condition at a given time, and one may arrange a number of prints on a card to illustrate a sequence of changes over a period of time.

It is a simple matter for the photographer to copy the prints on Kodachrome film, singly or in groups, and the resulting transparencies in single or multiple form may then be projected. Thus a single slide may be presented to a class to show the progress of a fundus lesion. It is true, however, that a copy made in this manner will not reproduce the color as perfectly as in the original print, owing to the natural limitations of all color reproduction processes. The older method, requiring Minicolor prints from the original Kodachrome transparency, could answer the same purpose, but I feel that the Kodacolor method is simpler.

The Kodacolor negative does not form a transparency suitable for viewing directly, since the color values as well as the tone relations are reversed so that a color positive can be obtained during a subsequent printing process. The dyes used in the Kodacolor process (as well as

in the Kodachrome process) are as stable as possible for the rather exacting purposes in color photography, but, like other dyes, may in time change. It is advisable, therefore, not to allow the prints to remain in bright light for long periods.

I have not exposed Kodacolor film in the Zeiss-Nordenson camera, which employs the tungsten lamp in place of the arc. I believe, however, that to do so would be feasible. The resultant pictures would be some-



A, Kodacolor print of a normal fundus reproduced in black and white to show the difference in size between the original negative and the enlarged color picture. *B* and *C*, black and white prints from Kodacolor negatives.

what redder than those obtained by my method, although it is likely that filter compensation could be used satisfactorily.

This paper was submitted to Mr. H. L. Gibson, of the Eastman Kodak Company, for criticism, and he made valuable constructive suggestions for the application of this new type film to fundus photography.

Mr. Gibson does not advise that Kodachrome transparencies be entirely discarded as a medium of photographic color rendition of the fundus, especially since Minicolor prints are available.

I quote from Mr. Gibson's letter the following extract, which is concerned with Kodacolor film and color photography in general:

> No process of color photography now in existence can reproduce the colors of the original subject with photometric accuracy. This is due in part to certain limitations in the spectral reflectances or transmissions of primary dyes and pigments used to build up the color image. Also, the layers bearing the three primary colors are subject to slight variations in coating of the emulsions, in storing of the films and in processing of the films. Hence, any system of color photography must necessarily be a combination of compromises. That these compromises can be made so that only slight variations in color accuracy and reproducibility may occur is attested by the acceptance of color photography in scientific, commercial and personal picture taking. In the latter two applications, limitations in the form of possible minor deviations from absolute accuracy in color rendering are no disadvantage in practice. However, we feel that a discussion of any process of color photography in connection with scientific uses should make clear that, while color photography is extremely valuable in most instances, there may be occasions when extreme color accuracy and reproducibility should be approached from a tentative viewpoint. Such a presentation is acceptable to scientific men because they are accustomed to weighing various data carefully.
>
> If the value of color photographs of the fundus lies in depicting color differences, such as those encountered between superficial blood vessels and the other structures, then we feel that Kodacolor photography would be perfectly satisfactory. However, should a general over-all color be of significance, such as that which may be evidenced during various stages of an inflammation (especially if the stages are photographed on different rolls of film at different times), then we feel that the limitations of color photography should be taken into account.

The method described of recording the ocular fundus in color by the use of Kodacolor roll film, through the excellence of its prints, makes this film a valuable addition to the equipment of the ophthalmologist who uses the Nordenson fundus camera.

20 East Fifty-Third Street.

Clinical Notes

USE OF ZELEX IN MAKING IMPRESSIONS OF THE EYE FOR MOLDED CONTACT GLASSES

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The use of molded contact glasses has largely superseded the use of ground contact glasses because the final results are better with the former method. The taking of a true impression, or negative, of the anterior ocular calotte is a fundamental procedure in this method. It is an important procedure because, a perfect negative having been obtained, the manufacture of the molded contact glass is a relatively easy matter.

Factors which interfere with the taking of a true negative of the cornea and sclera are (*a*) unsuitability of the plastic material, (*b*) movements of the eye while the impression is being taken, (*c*) pliability of the tissues of the eye and the formation of folds in the conjunctiva, (*d*) changes in the shape of the negative before the positive cast is made and changes in its shape while the negative is being dislodged from the eye and (*e*) episcleral and conjunctival pathologic changes which may affect the shape of the anterior ocular segment. The last group of factors can be dismissed by being regarded as contraindications to the immediate fitting of contact lenses.

Factors such as the pliability of the ocular bulb and movements of the eye during the procedure cannot be eliminated totally, but when due care is taken they can be reduced to a minimum. The selection of a suitable plastic material for taking of the negative will greatly facilitate the procedure. An ideal medium should embody the following properties: (*a*) it should be quick setting; (*b*) being chemically inert, nonabrasive and soft, it should not irritate the eye, and (*c*) it should not change its shape or size within a certain period and if deformed during dislodgment from the eye should be sufficiently elastic to regain its original form. The technic with such a medium will be simple.

Many different kinds of impression mediums have been used, the chief ones being negocoll and dental wax (gage 20). The technic with negocoll has been described by Thier,[1] while the use of dental wax was introduced by Town.[2] Both methods are unreliable in their results and are time consuming. The negatives are not elastic. The eye, being pliable, can alter slightly in shape when the dental wax is being pressed against it. Further aberration from the true shape of the anterior ocular segment can occur when the wax or negocoll mold is dislodged from the eye, because the slightest deformation (not only indentation)

1. Thier, P. F. X.: Individually Moulded Protheses, Ophthalmologica **99**:500, 1940.

2. Town, A. E.: Impression Technic for Contact Glasses, Arch. Ophth. **23**:822 (April) 1940.

of the material persists in the final issue. These mediums are not elastic enough to reassume their former shapes. The slightest deformation may produce a clinically bad fit.

I should like to communicate my experience with a new plastic substance, zelex, which is described by the manufacturer [3] as a "flexible colloidal material." It is marketed as a fine pinkish powder which does not deteriorate on storage. This powder does not impart a gritty sensation if introduced into an unanesthetized conjunctival sac. In powder or paste form zelex has no chemical or physical reaction on the eye. It dissolves easily in hot or cold water and takes a short time to set into a firm elastic mold. The setting time depends on the temperature of the water. If the water is cold (50 to 60 F.) the setting process takes ten to fifteen minutes, while at temperatures between 85 and 98 F. the setting time is three to six minutes. With water of the two temperatures the powder was dissolved in its own weight of water. This proportion of water and powder produces a paste of optimum viscosity for ophthalmologic use. The proportion of powder and water, as well as the temperature of the water, can be varied, depending, respectively, on the consistency of the paste and the setting time required by the operator.

For ophthalmologic purposes one requires a quick-setting paste which is so soft that it will fill every indentation of the conjunctival and corneal surfaces. I usually mix equal quantities of water and powder by weight at a temperature of 105 to 108 F. The eye is cocainized and the head of the patient is put back so that if he fixes a given light source an equal area of sclera is to be seen in each fornix. The soft paste is now ladled into the conjunctival sac while the lids are retracted and lifted slightly off the eyeball. One must be careful not to introduce bubbles of air with the material. To eliminate such bubbles and at the same time obtain a good "over-all" mold, one can fill a large contact glass with the paste and then apply it to the eye. If the eye now moves, the contact glass and the paste move with the eye. A small rubber sucker is applied to the contact glass, and the mold is removed from the eye. During the removal of the mold one need have no fear of deformation of the negative, because the substance is flexible and elastic and if deformed immediately reassumes its former shape. It is advisable to cast the positive mold as soon as possible, because after three hours the plastic mold begins to dry and shrink. For the positive mold, dental stone is preferable to plaster of paris because it is harder, and it is as easy to use. If there are any large conjunctival folds, they can be trimmed away carefully on the positive cast.

This colloidal material is eminently suitable because of such properties as a variable consistency of the paste, a short setting time, elasticity of the mold and inertness of the mold when in contact with ocular tissues. I have the idea that it absorbs the local anesthetic rapidly, because in cases in which I have had to make a second or third impression I have had to instil more of the local anesthetic to ensure absence

3. Zelex is manufactured by the Amalgamated Dental Co., Ltd., London, and by the L. D. Caulk Company, Milford, Del. It is used for impressions of the mouth taken prior to fitting artificial dentures.

of blepharospasm. This substance is also suitable for the taking of impressions for individually molded prostheses as suggested by Thier.[1] Thier used negocoll. I suggest that zelex is more suitable for this purpose than negocoll. The taking of a zelex negative is a matter of minutes.

I advocate that this easily used and satisfactory material for the taking of impressions of the eye be used not only because of the simplicity of the technic and the shortness of the time necessary for the procedure but because of the accuracy of the impression obtained.

Ophthalmologic Reviews

EDITED BY DR. FRANCIS HEED ADLER

VIRUSES AND VIRUS DISEASES OF EYE

I. PROPERTIES AND NATURE OF VIRUSES

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NEW YORK

Early workers in microbiology used the term virus in a broad sense to indicate any specific agent of infectious disease. In recent years, however, use of the term has been limited to a group of agents lying near or below the limits of resolution of the ordinary compound microscope which are usually able to pass filters retaining ordinary bacteria and which can be cultivated apart from the animal or plant body only in the presence of living cells.

In this restricted sense the viruses, like bacteria, fungi, protozoa, spirochetes and Rickettsia, form a group of disease agents having fundamental properties in common. That no group has greater economic or hygienic importance is apparent from the fact that the inciting causes of such diseases as poliomyelitis, the common cold, influenza, trachoma and yellow fever are viruses. Knowledge concerning them has increased rapidly in the last two decades, with the result that the properties of typical viruses, such as vaccinia virus or tobacco mosaic virus, can be defined almost as well as those of any specific bacterium. It is proposed in this review to consider in part I the nature and properties of viruses in general and in part II those viruses and their properties which are of ocular significance.

A. PROPERTIES OF VIRUSES

Viruses have three principal characteristics which distinguish them from other microbic forms: (1) They are able to pass filters which retain all ordinary bacteria; (2) they are obligate cell parasites, unable to multiply apart from living cells, and (3) most of them produce cytoplasmic or nuclear inclusion bodies in susceptible cells.

Filtrability.—Although Pasteur, on the basis of his study of rabies, postulated the existence of invisible living agents of disease, it was the discovery that some such agents could pass through porcelain and

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diatomaceous earth filters that first focused attention on what are now known as viruses. With refinements in filtration technic, particularly through the development by Elford [1] of a series of collodion membranes with graded pore diameters, it became possible to measure the size of virus particles with a considerable degree of accuracy. After the largest pore diameter which serves to retain any given virus is determined, the particle size is estimated from a calibration curve based on filtrations made with particles of known size. Thus the limiting pore diameter for vaccinia virus is 250 millimicrons and the estimated particle size 150 to 180 millimicrons (Elford [2]). Most of the known viruses have been measured by this method (fig. 1), and it has been established that particle size varies over a wide range from the 250 millimicron average size of psittacosis virus to the 10 millimicron average size of foot and mouth disease virus.

The particle size of viruses has also been measured by direct visual observation in the case of the large viruses, such as those of psittacosis and trachoma; by photography with ultraviolet light [3] or the electron microscope,[4] in the case of viruses too small to be resolved with ordinary light, and by centrifugation analysis.[5] According to the last method the size of the particles in an unknown suspension is determined from the sedimentation velocity observed under conditions under which Stokes's law is valid. There has been a reasonable agreement as to results among these several methods of estimating particle size; e. g., the size of vaccinia virus is 125 to 175 millimicrons according to ultrafiltration analysis,[2] 150 to 170 millimicrons according to photography with ultraviolet light [6] and 170 to 180 millimicrons according to centrifugation analysis.[7] Chambers and Henle,[8] however, have claimed recently that influenza A

1. Elford, W. J.: New Series of Graded Collodion Membranes Suitable for General Bacteriological Use, Especially in Filterable Virus Studies, J. Path. & Bact. **34**:505, 1931.

2. Elford, W. J.: Filtration of Vaccinia Virus Through Gradocol Membranes, Brit. J. Exper. Path. **13**:446, 1932.

3. Barnard, J. E., in Discussion on the Microscopy of the Filtrable Viruses, J. Roy. Micr. Soc. **52**:233, 1932. Barnard, J. E., and Welch, V. F.: Fluorescence Microscopy with High Powers, ibid. **56**:361, 1936.

4. von Borries, B.; Ruska, E., and Ruska, H.: Bakterien und Virus in übermikroskopischer Aufnahme (mit einer Einführung in die Technik des Übermikroskops), Klin. Wchnschr. **17**:921, 1938.

5. Elford, W. J.: Centrifugation Analysis, in Doerr, R., and Hallauer, C.: Handbuch der Virusforschung, Berlin, A. Hirschwald, 1938, p. 195.

6. Barnard, J. E.: Microscopical Evidence of Existence of Saprophytic Viruses, Brit. J. Exper. Path. **16**:129, 1935.

7. Elford, W. J., and Andrewes, C. H.: Centrifugation Studies: Viruses of Vaccinia, Influenza, and Rous Sarcoma, Brit. J. Exper. Path. **17**:422, 1936.

8. Chambers, L. A., and Henle, W.: Concentration, Isolation and Determination of the Size of the Virus of Influenza A, Science **94**:551, 1941.

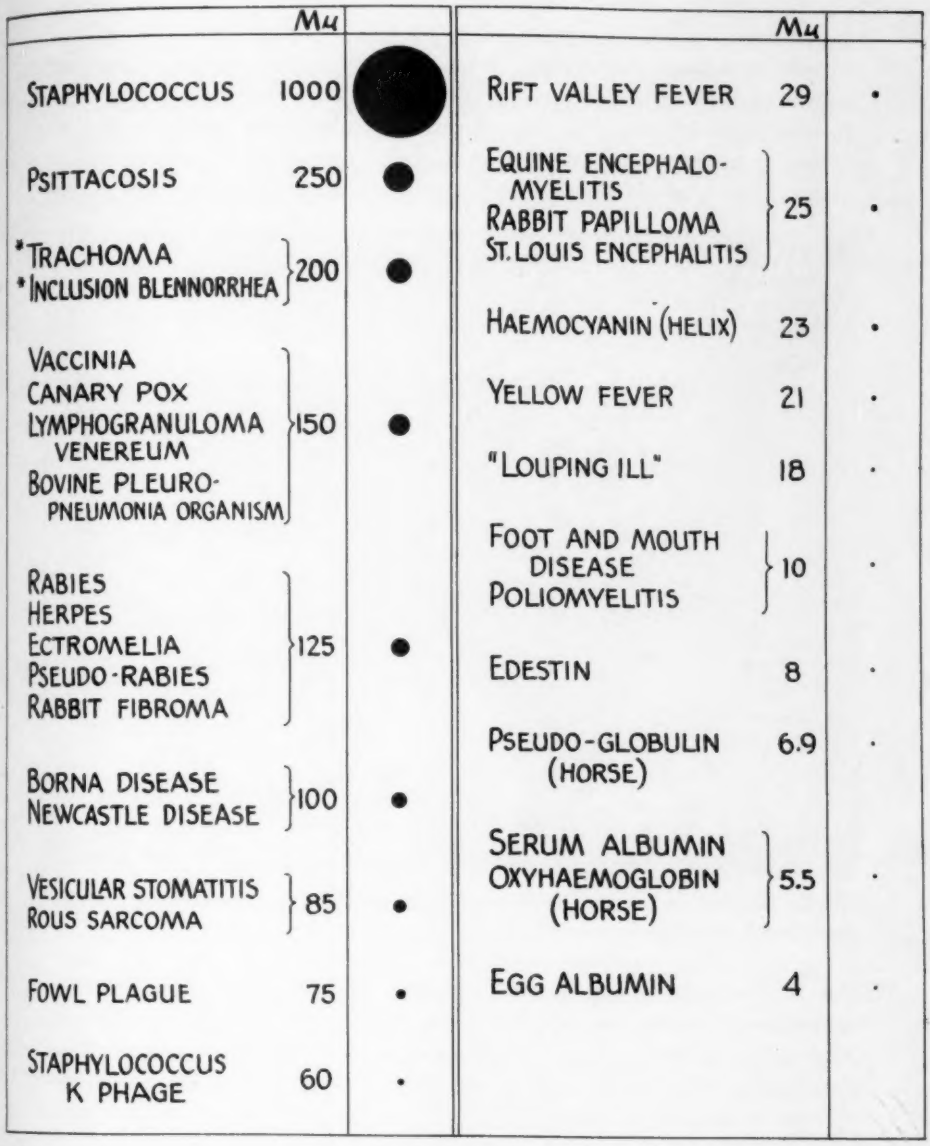

Fig. 1.—Particle size of viruses compared with the size of bacteria and protein molecules (compiled from data on filtrations as summarized by W. J. Elford in Doerr, R., and Hallauer, C.: Handbuch der Virusforschung, Berlin, A. Hirschwald, 1938).

virus is appreciably smaller according to studies with the electron microscope than the size previously estimated from filtration studies.

The electron microscope has recently assumed further importance in the investigation of viruses by virtue of its usefulness in the study of viruses and their antiserums. Thus, Anderson and Stanley [9] analyzed mixtures of tobacco mosaic virus with (1) normal serum, (2) antiserum to tomato bushy stunt, (3) antiserum to potato latent mosaic, (4) antiserum to tobacco ring spot viruses and (5) antiserum to tobacco mosaic virus. The analysis showed that asymmetrically shaped molecules from

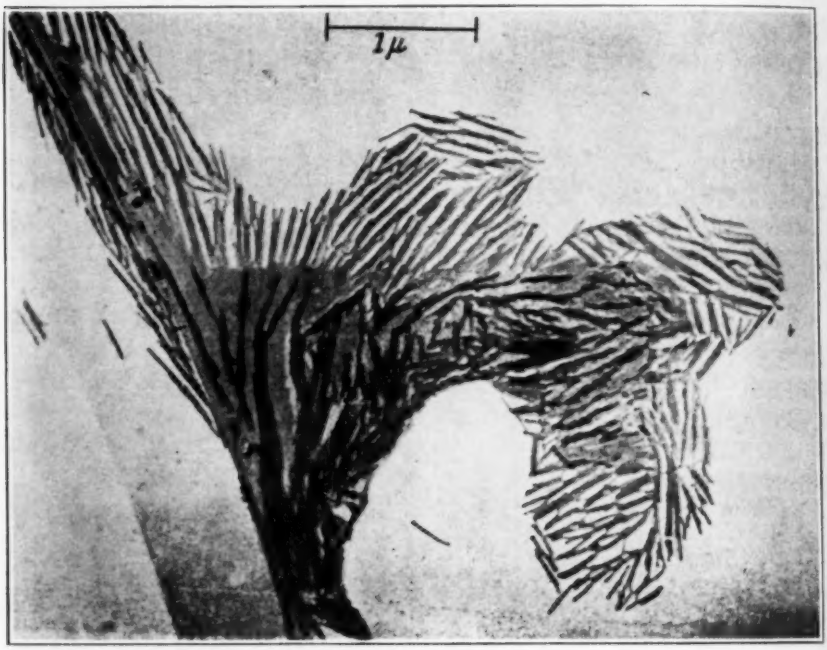

Fig. 2.—Tobacco mosaic virus as revealed by the electron microscope (× 24,600; from Stanley and Anderson [11]).

the homologous serum reacted specifically with the virus particles, whereas molecules from normal serum or from other antiserums did not. The optics of the electron microscope have recently been detailed by Zworykin,[10] who stated that the instrument at its present stage of development is capable of resolving objects at least fifty times smaller than

9. Anderson, T. F., and Stanley, W. M.: Study by Means of Electron Microscope of Reaction Between Tobacco Mosaic Virus and Its Antiserum, J. Biol. Chem. **139**:339. 1941.

10. Zworykin, V. K.: Image Formation by Electrons, Sigma Xi Quart. **29**:3, 1941.

11. Stanley, W. M., and Anderson, T. F.: Study of Purified Viruses with the Electron Microscope, J. Biol. Chem. **139**:325, 1941.

can be seen with the best conventional microscope. Figure 2, taken from a report by Stanley and Anderson,[11] illustrates the pencil-like form of tobacco mosaic virus as revealed by the electron microscope, and figure 3, taken from a report by von Borries, Ruska and Ruska,[4] illustrates the oval shape of the virus of infectious myxomatosis.

Cytotropism.—The term cytotropism has been applied by Goodpasture[12] to the obligate cell parasitism of viruses. No true virus has ever been grown apart from living cells, the few claims made for the cultivation of viruses in cell-free mediums having all been shown to be erroneous. Multiplication of viruses outside the body, however, has been achieved by tissue culture methods. Most viruses will multiply in tissue cultures of susceptible cells, but there are a few, in particular the viruses of molluscum contagiosum, trachoma and inclusion blennorrhea, which

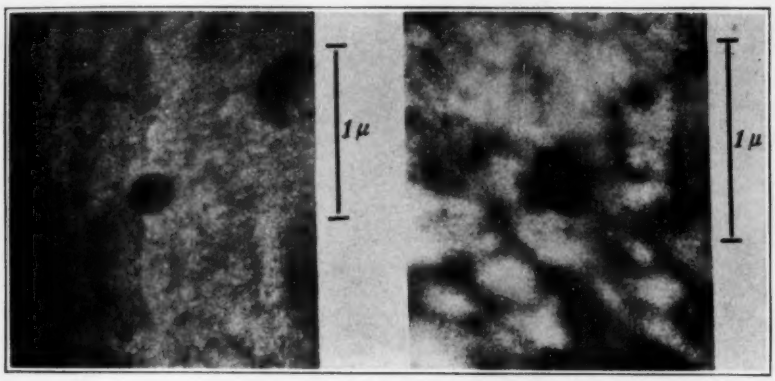

Fig. 3.—Virus of infectious myxomatosis as seen with the electron microscope (× 19,000 and 22,000; from von Borries, Ruska and Ruska[4]).

have so far resisted cultivation[13] even in their normal host cells (i. e., human cutaneous, conjunctival and corneal epithelium), whether resting or multiplying. In this connection it is well known that certain viruses, such as herpes simplex virus, grow best on actively multiplying cells, while others, such as vaccinia virus, prefer resting tissues.

Cells of the chick embryo have been found particularly useful for cultivation of viruses, not only because of the ease and relative inexpensiveness with which they may be obtained but because of the great

12. Goodpasture, E. W.: (*a*) Etiological Problems in the Study of Filtrable Virus Diseases, in Harvey Lectures, 1929-1930, Baltimore, Williams & Wilkins Company, 1931, p. 77; (*b*) Cytotropic Viruses, with References to Filterable Forms of Bacteria and Cancer, Am. J. Hyg. **17**:154, 1933.

13. Thygeson, P., and Richards, P.: Nature of the Filtrable Agent of Trachoma, Arch. Ophth. **20**:569 (Oct.) 1938.

number of viruses which grow readily on them. In addition to the tissues of the embryo itself, those of the embryonic membranes, the chorioallantois and the amnion, have been employed with success. Figure 4 illustrates the proliferative foci characteristic of the growth of herpes simplex virus on the chorioallantois.

Formation of Inclusion Bodies.—The formation of inclusion bodies is one of the most characteristic features of the viruses, and the occurrence of inclusions in cells is now considered an almost certain indication of virus activity. These virus bodies are either intranuclear or intracytoplasmic, and many of them are sufficiently characteristic, e. g. the

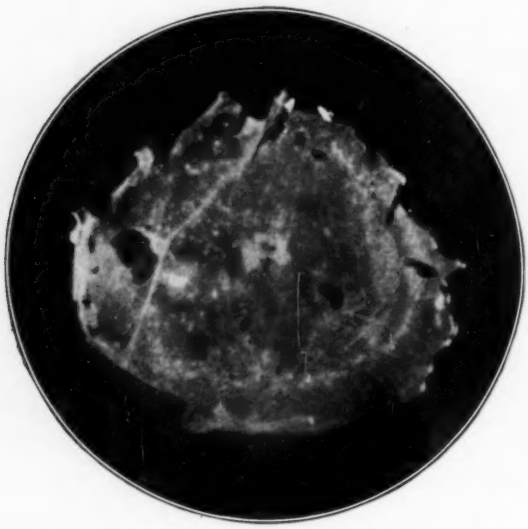

Fig. 4.—Proliferative lesions on the chorioallantoic membrane of a developing chick embryo caused by herpes simplex virus.

Negri bodies of rabies, to be of importance in the microscopic diagnosis of the disease in which they occur.

The exact nature of the inclusion bodies has excited much speculation. Early workers, influenced by the discovery of the malarial parasite and its life cycle, regarded the inclusions as protozoa and even described complicated life cycles for them, but the protozoal theory became untenable when the diseases in which inclusions could be demonstrated were shown to be transmissible by filtrates. It was then generally believed that the inclusions represented intracellular pathologic changes resulting from virus action. A few of the early workers, notably Prowazek [14] and

14. Prowazek, S.: Chlamydozoa: I. Ausammenfassende "Ubersicht.," Arch. f. Protistenk. **10**:336, 1907.

Lipschutz,[15] held that inclusions were essentially microcolonies of viruses masked by a reaction product of cell origin, and this theory gained widespread acceptance for the cytoplasmic inclusions on the basis of the experimental work of Goodpasture and his associates [16] on the Bollinger bodies of fowl pox. These investigators were able to obtain inclusions free from cells by teasing out small bits of tissue or, better, by dissolving the cell structure with an alkaline solution of commercial trypsin. They were then able to show that the bodies, after having been allowed to swell in distilled water for from thirty minutes to one hour, consisted of two component elements: (1) a hyaline-like matrix having the appearance of a honeycomb of minute cells and (2) myriads of minute particles in brownian motion embedded in these minute cells, one particle to a cell. An isolated inclusion when crushed and stained to show virus particles revealed them in numbers proportionate to the number of tiny dancing particles observed in the fresh preparations. By means of the microdissection apparatus these investigators were able to show further that the inclusions were totally and fractionally infective.

The majority of cytoplasmic inclusion bodies have since been shown to have this dual structure of elementary virus particles and matrix, the latter being in all probability a cell reaction product whose chemical constitution varies with the different viruses. Thus the matrix of the Guarnieri body of vaccinia is known to contain thymonucleic acid,[17] the Bollinger body of fowl pox to contain a lipoid constituent which blackens with osmic acid [18] and the Halberstadter-Prowazek body of trachoma to contain glycogen as its principal constituent.[19] The matrix materials of most inclusions stain with ordinary histologic dyes in such a manner as to mask their component virus particles, which become visible only after mechanical or chemical disruption of the inclusion, but the composition of the matrixes of the inclusions of psittacosis, lymphogranuloma venereum, trachoma and inclusion blennorrhea is such as to allow a clear view of the embedded virus particles.

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15. Lipschutz, B.: Untersuchungen uber die Aetiologie der Krankheiten der Herpesgruppe (Herpes zoster, Herpes genitalis, Herpes febrilis), Arch. f. Dermat. u. Syph. **136**:428, 1921.

16. Woodruff, C. E., and Goodpasture, E. W.: The Infectivity of Isolated Inclusion Bodies of Fowl-Pox, Am. J. Path. **5**:1, 1929. Goodpasture, E. W.: Cellular Inclusions and the Etiology of Virus Diseases, Arch. Path. **7**:114 (Jan.) 1929.

17. Findlay, G. M.: Comparison Between the Inclusions of Alastrim and Variola Vera in Man, in Doerr, R., and Hallauer, C.: Handbuch der Virusforschung, Berlin, A. Hirschwald, 1938, p. 298.

18. Goodpasture,[12a] p. 99.

19. Rice, C. E.: The Carbohydrate Matrix of the Epithelial-Cell Inclusion in Trachoma, Am. J. Ophth. **19**:1, 1936. Thygeson, P.: Matrix of Epithelial Cell Inclusion Body of Trachoma, Am. J. Path. **14**:455, 1938.

Although there is no reason to suppose that intranuclear inclusions differ in composition from cytoplasmic inclusions, the only evidence of their identity of structure so far advanced has been with respect to the viruses of herpes simplex and herpes zoster. Nicolau [20] and Nicolau and Kopciowska [21] stated that by special stains they have been able to demonstrate virus particles in the nuclear inclusions of these two diseases. In general it may be stated that intranuclear inclusions are less specific than cytoplasmic inclusions, and while two types, called A and B by Cowdry,[22] are recognized, no virus disease can be diagnosed with certainty solely from the appearance of its intranuclear inclusions. Intranuclear changes resembling inclusion bodies appear to have been induced by nonspecific means (Olitsky and Harford [23] and Duke-Elder [24]), but the possibility that a latent virus was activated by these means must still be considered.

Figure 5 illustrates the inclusion bodies, both cytoplasmic and intranuclear, which are found in cases of virus infections of the eye and its adnexa.

Existence of Free Elementary Bodies.—Contrary to the popular belief that all viruses are necessarily ultramicroscopic, it is now known that many of the larger viruses can be seen under the ordinary compound microscope when good oil immersion lenses and proper illumination are employed. The larger virus particles, generally known as elementary bodies, are best seen when suitably stained. The elementary bodies of psittacosis, lymphogranuloma venereum, trachoma (fig. 6) and inclusion blennorrhea can be stained with simple stains, such as the Giemsa stain, but the others require use of a mordant or prolonged staining. Among the latter are the elementary bodies of canary pox, ectromelia, fowl pox, herpes simplex, infectious myxomatosis, molluscum contagiosum, rabbit fibroma, vaccinia and variola, herpes zoster and varicella. It is noteworthy that the use of a mordant may as much as double the apparent

20. Nicolau, S.: Le mécanisme de la formation des inclusions dans le système nerveux des lapins infectés experimentalement avec le virus herpetique, Compt. rend. Soc. de biol. **126**:326, 1937.

21. Nicolau, S., and Kopciowska, L.: La morphologie de l' inframicrobe herpétique dans le tissu des animaux infectés expérimentalement et le mécanisme de la formation des inclusions qu' il engendre dans les cellules, Ann. Inst. Pasteur **60**:401, 1938.

22. Cowdry, E. V.: Problem of Intranuclear Inclusions in Virus Diseases, Arch. Path. **18**:527 (Oct.) 1934.

23. Olitsky, P. K., and Harford, C. G.: Intranuclear Inclusion Bodies in Tissue Reactions Produced by Injections of Certain Foreign Substances, Am. J. Path. **13**:729, 1937.

24. Duke-Elder, W. S., and Duke-Elder, P. M.: Histological Study on Action of Short-Waved Light upon Eye, with Note on "Inclusion Bodies," Brit. J. Ophth. **13**:1, 1929.

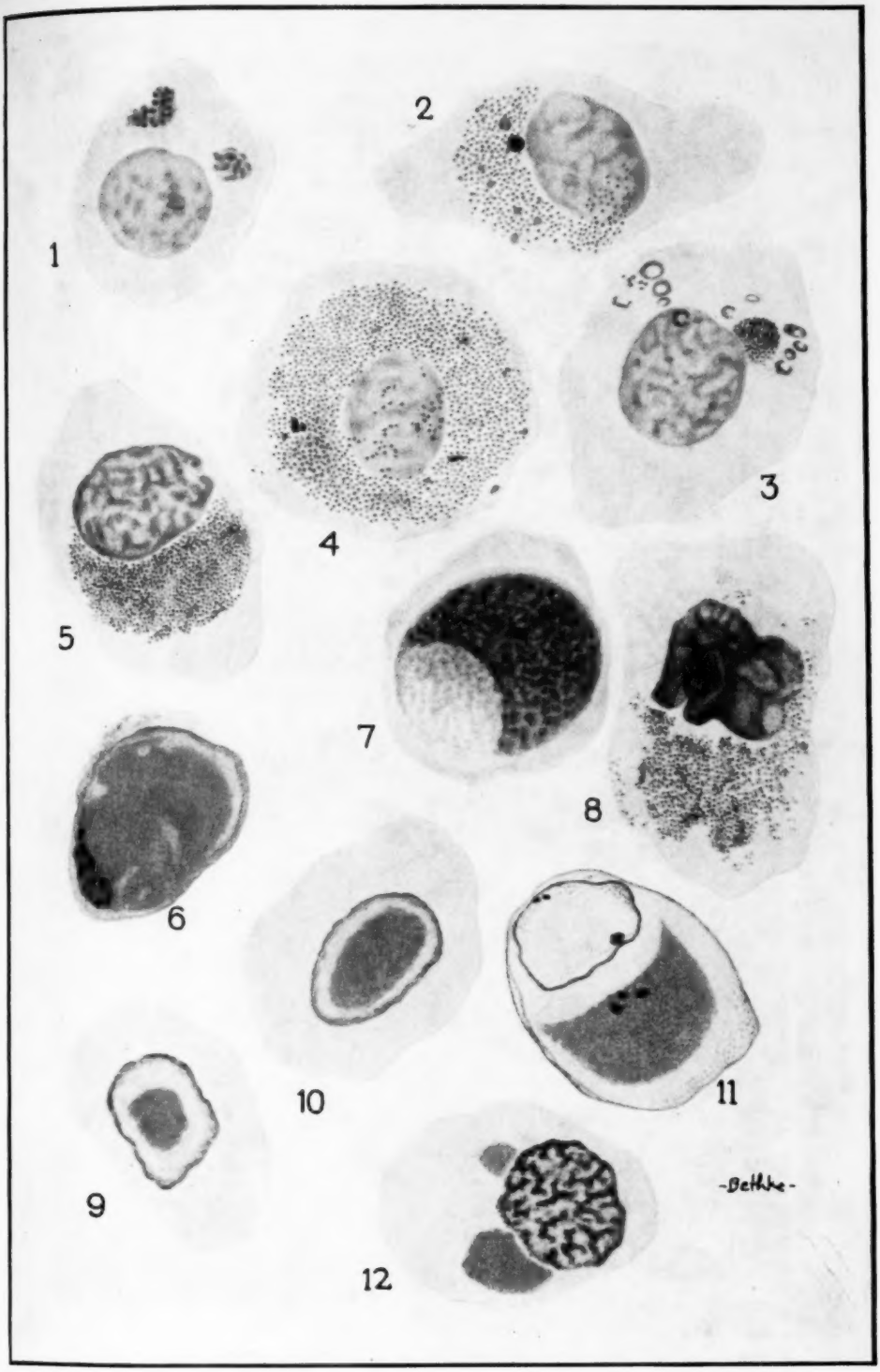


Fig. 5.—Inclusion bodies of ocular importance: *1*, small initial body inclusion of inclusion blennorrhea; *2*, mixed elementary and initial body inclusion of inclusion blennorrhea; *3*, small initial body inclusion of trachoma; *4*, large elementary body inclusion of trachoma; *5*, elementary body inclusion of trachoma; *6*, cytoplasmic inclusion of molluscum contagiosum; *7*, trachoma inclusion, iodine stain, showing carbohydrate matrix; *8*, inclusion of lymphogranuloma venereum; *9*, intranuclear inclusion of herpes simplex; *10*, intranuclear inclusion of herpes zoster; *11*, cytoplasmic inclusion of infectious myxomatosis; *12*, cytoplasmic inclusion (Guarnieri body) of vaccinia.

size of the virus particle. By this means certain viruses which lie below the resolving power of the microscope when unstained can be rendered visible.

Other Properties of Viruses.—Tissue Affinities: Viruses appear to have somewhat greater affinities for particular tissues than bacteria have. While certain ones, such as vaccinia virus, are capable of infecting cells of ectodermal, mesodermal and entodermal origin in a wide range of animal hosts, others, such as molluscum contagiosum virus, can develop only in one particular host and in one particular cell type, in this case

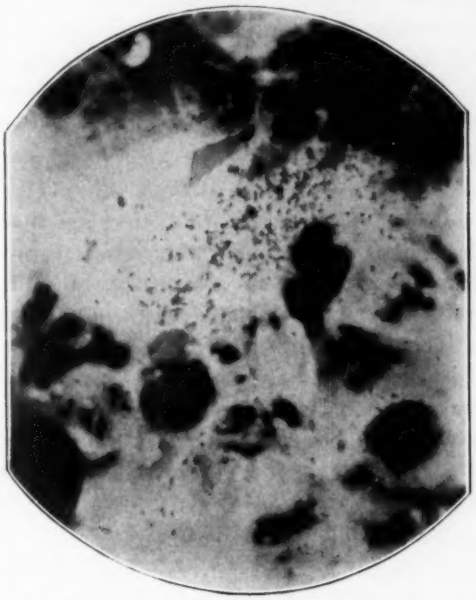


Fig. 6.—Elementary bodies of trachoma (Giemsa stain; × 1,500).

ectodermal epithelium of man. Many viruses show a definite if not absolute affinity for the skin and others for tissues of the nervous system; the dermotropic viruses are represented by the agents of the common wart, vaccinia, variola, varicella, molluscum contagiosum, etc.; the neurotropic viruses, by the agents of rabies, poliomyelitis, Borna disease, St. Louis encephalitis, etc. Certain viruses have an affinity for particular organs, e. g., the affinity of the virus of mumps for the parotid gland, of the agents of influenza and psittacosis for the lungs and of the agent of trachoma for the eye. Certain viruses, e. g., those of leukemia of chickens and of infectious anemia of horses, are hemotropic.

Shape of Virus Particles: Considerable information regarding the shape as well as the size of virus particles has accumulated from direct

visual and photographic observation and from ultrafiltration and ultracentrifugation. By these means it has been learned that most of the animal viruses are spherical in shape and remarkably uniform in size. Their uniformity of size is clearly indicated for a typical virus, such as vaccinia virus, by the sharp filtration end point obtained with graded collodion membranes and by the relatively sharp sedimenting boundary obtained during centrifugation of a purified suspension.[25] Atypically, the virus of tobacco mosaic has been shown by means of the electron microscope [11] to have the form of a slender rod about 15 millimicrons in diameter and 150 millimicrons in length, a form which had already been postulated on the basis of indirect methods of examination. The viruses of trachoma, inclusion conjunctivitis, psittacosis and lymphogranuloma venereum exhibit a regular sequence of changes varying from the elementary body, which is spherical and uniform in size, to a larger coccobacillary bipolar-staining nonfiltrable form which may be over a micron in length.

Mutation, Variation and Adaptations: Viruses, like bacteria, are able at times to change their characteristics and to adapt themselves to new conditions. Rabies virus, for example, which was formerly considered a strictly neurotropic virus, has been adapted by Levaditi and Schoen [26] to the corneal epithelium of the rabbit and to the epithelial cells of the Pearce tumor. A classic example of virus mutation is seen in the transformation of rabies street virus into fixed virus. The same phenomenon is apparent in the transformation of smallpox virus into vaccinia virus, a change which appears to be irreversible, and in the apparently permanent loss of virulence for man of yellow fever virus after repeated passage through tissue cultures.[27]

Resistance to Physical and Chemical Agents: In contrast to its unfavorable action on most bacteria, glycerin has been found to have a conserving effect on most viruses. Desiccation *in vacuo* at low temperatures has also found wide application in the preservation of viruses, although certain ones, such as trachoma virus, are destroyed rapidly by drying. All viruses are inactivated by high temperatures, but the majority resist low temperatures well. Like the bacteria, viruses show a variable resistance to chemical agents. It is noteworthy that bile has a

25. Pickels, E. G., and Smadel, J. E.: Ultracentrifugation Studies on Elementary Bodies of Vaccine Virus: General Methods and Determination of Particle Size, J. Exper. Med. **68**:583, 1938.

26. Levaditi, C., and Schoen, R.: Evolution du virus vaccinal et du virus rabique des rues dans l' epithelium cornéen, Compt. rend. Soc. de biol. **119**:706, 1935.

27. Lloyd, W.; Theiler, M., and Ricci, N. I.: Modification of Virulence of Yellow Fever Virus by Cultivation in Tissues in Vitro, Tr. Roy. Soc. Trop. Med. & Hyg. **29**:481, 1936.

rapid destructive action on many viruses.[28] None of the typical viruses has been proved to be susceptible to any chemotherapeutic agent, but such atypical viruses as trachoma virus,[29] inclusion blennorrhea virus [30] and lymphogranuloma venereum virus [31] have been shown to be strikingly sensitive to sulfanilamide.

Cellular Changes Effected by Viruses.—In view of the intimate association of viruses with cells it is understandable that cellular changes should be a prominent feature in virus disease. In addition to forming inclusion bodies, viruses may provide stimuli resulting in cellular changes varying from the extreme of rapid cellular death, in the case of yellow fever virus, to the extreme of pure cellular proliferation, effected by Rous sarcoma virus and other viruses producing filtrable tumors. A state of symbiosis between the virus and the host cells may exist which allows persistence of the virus in the body for long periods in the absence of clinical symptoms. This is the case with herpes simplex virus.

The fact that a number of tumors, such as the common wart, molluscum contagiosum, the Rous sarcoma, Shope's fibroma and papilloma of rabbits, infectious myxomatosis and adenocarcinoma of frogs,[32] are known to be of virus origin indicates the possibility of a virus causation for malignant processes in human beings. As yet no human cancer has ever been transmitted by a cell-free filtrate, but this fact might conceivably be due to a masking of the virus by antibody, a phenomenon which occurs not infrequently during the recovery stage of typical virus infections. The virus theory of cancer postulates the occurrence of tumor viruses, widely distributed in the animal kingdom, which are normally latent but which may be activated by some stimulus, such as the application of a carcinogenic hydrocarbon (Andrewes [33]). However, except for the fact that certain latent viruses, such as Virus III and herpes simplex virus, do occur and can be activated by various stimuli, such as serial passage, or fever, there is little evidence to support this hypothesis.

The recent work of Syverton, Berry and Warren [34] on the Shope papilloma virus is of importance in this connection. This virus is the

28. Smith, W. L.: Action of Bile Salts on Viruses, J. Path. & Bact. **48**:557, 1939.

29. Loe, F.: Sulfanilamide Treatment of Trachoma: Preliminary Report, J. A. M. A. **111**:1371 (Oct. 8) 1938.

30. Thygeson, P.: Treatment of Inclusion Conjunctivitis with Sulfanilamide, Tr. Am. Ophth. Soc. **38**:111, 1940; Arch. Ophth. **25**:217 (Feb.) 1941.

31. MacCallum, F. O., and Findlay, G. M.: Chemotherapeutic Experiments on Virus of Lymphogranuloma Inguinale in Mouse, Lancet **2**:136, 1938.

32. Lucke, B.: Carcinoma in the Leopard Frog: Its Probable Causation by a Virus, J. Exper. Med. **68**:457, 1938.

33. Andrewes, C. H.: Latent Virus Infections and Their Possible Relevance to Cancer Problem, Proc. Roy. Soc. Med. **33**:75, 1939.

34. Syverton, J. T.; Berry, G. P., and Warren, S. L.: Roentgen Radiation of Papilloma Virus (Shope): Effect of X-Rays upon Papilloma Virus in Vitro, J. Exper. Med. **74**:223, 1941.

cause of infectious papillomas, common in wild rabbits, which may be transmitted in series by filtrates in wild rabbits but which produce only nontransmissible first generation papillomas in domestic rabbits. These nontransmissible warts often undergo malignant changes (Rous and Beard [35]), many of which eventually give rise to metastases in regional lymph nodes, the lungs and other internal organs. These secondary cancers are readily transplanted into a new rabbit host, and there is immunologic evidence of the continued presence of the Shope virus in the new tumors.[36] The nontransmissible papillomas of domestic rabbits respond favorably to roentgen rays, as do many noninfectious tumors, and the roentgenologic effect is due to direct action on the cells rather than on the virus, since cell-free virus requires several thousand times the tumor-destructive dose for its inactivation.[37]

For a discussion of this most interesting subject the reader is referred to the reviews by Andrewes,[33] Rous [38] and Rivers.[39]

While the primary changes in virus diseases are the result of direct action on parasitized cells, secondary effects on cells not directly infected by the virus do occur. Thus trachoma virus, which appears to be capable of parasitizing only conjunctival and corneal epithelium,[13] produces subepithelial changes leading to formation of follicles and necrosis and eventually to replacement of scar tissue. Remote changes in bacterial disease are known to be produced as a result of the liberation of soluble toxins, and it seems highly probable that remote changes in virus infections are produced by similar soluble toxins, although none have been demonstrated with certainty as yet. It is known, however, that certain viruses, including those of lymphogranuloma venereum,[40] vaccinia [41] and

35. Rous, P., and Beard, J. W.: Progression in Carcinoma of Virus-Induced Rabbit Papillomas (Shope), J. Exper. Med. **62**:523, 1935.

36. Kidd, J. G.; Beard, J. W., and Rous, P.: Serological Reactions with Virus Causing Rabbit Papillomas Which Become Cancerous: Tests of Blood of Animals Carrying Various Epithelial Tumors, J. Exper. Med. **64**:79, 1936.

37. Syverton, J. T.; Harvey, R. A.; Berry, G. P., and Warren, S. L.: The Roentgen Radiation of Papilloma Virus (Shope), J. Exper. Med. **73**:243, 1941. Syverton, J. T.; Berry, G. P., and Warren, S. L.: The Roentgen Radiation of Papilloma Virus (Shope), ibid. **74**:223, 1941.

38. Rous, P.: Virus Tumors and Tumor Problem, in Harvey Lectures, Baltimore, Williams & Wilkins Company, 1935-1936, p. 74.

39. Rivers, T. M.: Lane Medical Lectures: Viruses and Virus Diseases, Stanford Univ. Publ., Univ. Series, M. Sc. **4**:45, 1939.

40. Rake, G. M.; Shaffer, M. F.; Jones, H. P., and McKee, C. M.: Soluble Antigen in Lymphogranuloma Venereum, Proc. Soc. Exper. Biol. & Med. **46**:300, 1931.

41. Tulloch, W., in Discussion on Active Immunization in Virus Diseases, Proc. Roy. Soc. Med. **25**:452, 1931-1932. Craigie, J.: Nature of Vaccinia Flocculation Reaction, and Observations on Elementary Bodies of Vaccinia, Brit. J. Exper. Path. **13**:259, 1932.

infectious myxomatosis,[42] produce soluble antigens capable of reacting with specific antiserums.

Immunity in Virus Diseases.—There is a wide variation in the ability of viruses to induce immunity. Some of those which are strictly local in action and which attack only epithelium (e. g., the viruses of molluscum contagiosum and trachoma) are accompanied by no demonstrable immunity; the viruses of variola and varicella, on the other hand, produce immunity which is complete and lasting. Other viruses, such as the virus of foot and mouth disease, produce immunity lasting only a year or two, while the immunity produced by the viruses of the common cold and herpes simplex is even more transient. In some virus diseases, particularly in those of plants, permanent immunity is associated with persistence of the virus in the host tissues.

There is no reason to suppose that immunity in virus diseases differs in any fundamental respect from immunity in bacterial diseases. It is specific and is manifest in the blood stream in the form of reacting bodies which are comparable to agglutinins, precipitins and complement-fixing bodies and are capable of neutralizing the virus, of causing agglutination of virus particles or of producing a precipitation with virus-containing material. Along with the development of these circulating antibodies a cutaneous allergy may appear, and this, as in the case of the Frei test [43] in lymphogranuloma venereum, may be of prime importance in diagnosis.

Immunotherapy in Virus Diseases: Prophylactic immunization with virus vaccines is classically illustrated in the case of smallpox vaccination, in which an attenuated smallpox virus, i. e. vaccinia virus, serves to produce an effective immunity. Similarly, an effective vaccine against yellow fever has been developed by attenuating yellow fever virus by passage in tissue culture [27] so that it no longer produces clinical disease on injection into human beings. Prophylactic vaccination against rabies as usually employed consists in the use of rabies virus attenuated by drying. The use of completely inactivated viruses for vaccination has been attempted but has not met with great success.

There has as yet been no clearcut example of effective serotherapy of an established virus disease. Convalescent serum, on the other hand, has been employed with success in prophylaxis in the treatment of a number of diseases, including measles and varicella.

Plurality of Types: Viruses, like bacteria, may have a plurality of types. Thus, influenza virus rivals the pneumococcus in having multiple

42. Rivers, T. M., and Ward, S. M.: Infectious Myxomatosis of Rabbits: Preparation of Elementary Bodies and Studies of Serologically Active Materials Associated with Disease, J. Exper. Med. **66**:1, 1937.

43. Frei, W.: Eine neue Hautreaktion bei Lymphogranuloma Inguinale, Klin. Wchnschr. **4**:2148, 1925.

immunologic types, a factor which has made the problem of preparing an effective vaccine very complex.

Transmission of Viruses.—Among the viruses are to be found some of the most communicable of all disease agents (e. g., smallpox and measles viruses) as well as some of the least communicable (e. g., herpes zoster virus). Like bacteria, they are transmitted in a variety of ways. The virus diseases of the respiratory tract appear to spread by droplet transmission; others appear to spread by contact (e. g., molluscum contagiosum and the common wart), others venereally (e. g., lymphogranuloma venereum) and still others by arthropod vectors (e. g., yellow fever).

Latent Viruses.—Animals and plants may carry viruses within their cells without showing evidence of disease. The outstanding example is herpes simplex virus, which remains latent between attacks of fever blisters. The natural immunization which may be ascribed to latent or subclinical infection is exemplified in the case of yellow fever by the fact that, although large portions of the populations in tropical America and Africa have never suffered from clinical yellow fever, they show neutralizing antibodies in their serum. It has also been observed that during the course of influenza epidemics the serum of many persons shows substantial rises in neutralizing antibodies against the virus without appearance of the clinical disease. Psittacosis, a virus disease of birds, is known to produce a symptomless infection in certain species.[44] Finally, it is believed that the long-continued immunity which follows certain virus diseases may be due to persistence of the virus in the body.

Symbiosis of Viruses with Bacteria.—As has been shown by Shope,[45] the combination of swine influenza virus with Haemophilus suis is necessary for the production of swine influenza. Other viruses, such as measles virus, influenza virus and the virus of the common cold, may induce a nonspecific lowering of the resistance of the respiratory tract to secondary bacterial invaders.

B. NATURE OF VIRUSES

The early workers on viruses considered them to be minute microbes of a size below the limits of microscopic resolution. The subsequent demonstration of minute coccoid forms, now known as elementary bodies, in some virus diseases seemed further to substantiate the theory that

44. Meyer, K. F., and Eddie, B.: Ueber Papageienpest: Auf Grund von epidemiologischen und experimentellen Studien in Kalifornien, Klin. Wchnschr. **13**:865, 1934; Latent Psittacosis Infections in Shell Parakeets, Proc. Soc. Exper. Biol. & Med. **30**:484, 1933.

45. Shope, R. E.: Swine Influenza: Experimental Transmission and Pathology, J. Exper. Med. **54**:349, 1931.

viruses were microbic in nature. Although division forms of the elementary bodies were recognized, actual proof of their living nature by cultivation of them apart from living cells could not be obtained. This failure naturally led some observers to consider the possibility of their being nonliving cell products in the nature of autocatalytic enzyme-like agents. The finding, through differential filtration and ultracentrifugation studies, that certain viruses, such as those of poliomyelitis [46] and foot and mouth disease,[47] were of extremely small particle size (8 to 12 millimicrons), smaller in fact than some of the larger protein molecules, supported this possibility, for it seemed unlikely that the complex organization necessary for life could be contained in particles of such small size.

In 1935 Stanley [48] made the momentous announcement of the "isolation of a crystalline protein possessing the properties of tobacco mosaic virus." This announcement and its confirmation by other workers led many persons to decide that viruses were nonliving, because they considered it impossible for a living organism to take on a crystalline structure. However, as pointed out by Pirie,[49] crystallinity denotes simply a structural regularity, and no incompatibility between crystalline and living states actually exists. Nevertheless, this work of Stanley's focused attention on the chemical nature of viruses, and since 1935 proteins of high molecular weight having virus properties have been isolated by differential centrifugation or by chemical means in the case of a number of plant diseases [50] and in the case of the Shope rabbit papilloma.[51] As Stanley [52] has stated, protein structure may be expressed in many different ways, as in hormones, enzymes, toxins, etc., and since practically nothing is known about such structure, the identification of viruses with proteins adds but little to the understanding of their true nature. Chemical analysis has indicated, however, that

46. Theiler, M., and Bauer, J. H.: Ultrafiltration of Virus of Poliomyelitis, J. Exper. Med. **60**:767, 1934. Elford, W. J.; Galloway, I. A., and Perdrau, J. R.: Size of Virus of Poliomyelitis as Determined by Ultrafiltration Analysis, J. Path. & Bact. **40**:135, 1935.

47. Galloway, I. A., and Elford, W. J.: Filtration of Virus of Foot and Mouth Disease Through a New Series of Graded Collodion Membranes, Brit. J. Exper. Path. **12**:407, 1931.

48. Stanley, W. M.: Isolation of a Crystalline Protein Possessing the Properties of Tobacco-Mosaic Virus, Science **81**:644, 1935.

49. Pirie, N. W., in Needham, J., and Green, D. E.: Perspectives in Biochemistry, London, Cambridge University Press, 1937; cited by Stanley.[52]

50. Stanley, W. M.: Viruses Isolated by Ultracentrifugation, in Doerr, R., and Hallauer, C.: Handbuch der Virusforschung, Berlin, A. Hirschwald, 1938, p. 485.

51. Beard, J. W., and Wyckoff, R. W. G.: Isolation of Homogeneous Heavy Protein from Virus-Induced Rabbit Papillomas, Science **85**:201, 1937.

52. Stanley, W. M.: The Architecture of Viruses, Physiol. Rev. **19**:524, 1939.

the simplest viruses appear to be composed of protein plus nucleic acid; the more complex, of protein, nucleic acid and carbohydrate, and the most complex, of materials indistinguishable from those found in ordinary bacteria. It has been mentioned that at one end of the scale the larger viruses merge with some overlapping into the smaller bacteria, while at the other end the smaller viruses shade into the larger molecules.

Although the physical and chemical properties of the virus proteins are similar to those of ordinary proteins, the biologic properties are quite different. One of the fundamental properties of viruses is their infectiousness, i. e., their ability to multiply when introduced into living cells. This property of multiplication, which is the major property of living organisms, distinguishes viruses from even such biologically active enzymes as pepsin or trypsin, which show a sort of pseudomultiplication in that they can cause the autocatalytic conversion of specific inactive precursors, trypsinogen and pepsinogen, to trypsin and pepsin. Virus precursors have never been found in normal cells, and it seems extremely unlikely that they ever will be, in view of the multiplicity of precursors which would have to exist, a given host being capable of causing multiplication of any one of a multitude of different viruses or virus strains (Stanley [52]).

It would seem, therefore, that no fundamental differences between viruses and living organisms exist and that it would be safe to assume that viruses are simply the least complex members of a series of microorganisms which range from viruses and bacteria to protozoa and other higher forms of life. As has been suggested by Green,[53] Laidlaw [54] and others, viruses may well be looked on as minute bacteria which have lost substance and enzyme systems in becoming obligate cell parasites and are dependent on the metabolism of the host cell for all but certain highly specialized functions, such as reproduction and production of toxin.

The discussions on the nature of viruses have attracted wide attention because of their bearing on the nature and origin of life itself. The transition between the living and the nonliving must be a gradual one, and the boundary line, if one exists, may well lie close to the smaller viruses.

635 West One Hundred and Sixty-Fifth Street.

53. Green, R. G.: On Nature of Filtrable Viruses, Science **82**:443, 1935.

54. Laidlaw, P. P.: Virus Diseases and Viruses: Rede Lecture, 1938, New York, The Macmillan Company, 1938, p. 52.

News and Notes

EDITED BY DR. W. L. BENEDICT

SOCIETY NEWS

National Society for the Prevention of Blindness.—Dr. Mark J. Schoenberg, chairman of the glaucoma committee, is now in charge of the station for checking the accuracy of original Schiøtz tonometers which is maintained at the headquarters of the society, 1790 Broadway, New York. Dr. Adolph Posner, who formerly directed the tonometer-checking station, is on active duty with the Medical Corps, Army of the United States.

American Ophthalmological Society.— The seventy-ninth annual meeting will be held at the Homestead, Hot Springs, Va., on May 31, June 1 and June 2, 1943.

The members are requested to send to the chairman of the Program Committee, Dr. Walter I. Lillie, Philadelphia, as soon as possible, the titles and brief abstracts of such papers as they desire to present at the meeting. All titles and abstracts must be forwarded to Dr. Lillie before April 15, to be incorporated in the call for the meeting to be sent out May 1.

According to Article IV, Section 1, of the By-Laws, no paper shall be eligible for presentation at the meeting unless the title and an abstract are printed in the call for the meeting. This rule does not apply to the exhibition of new instruments or apparatus.

According to Article IV, Section 7, of the By-Laws, no paper submitted by a member in conjunction with a nonmember, by invitation, shall be read at any meeting of the society unless the member is present. If such a paper should be printed elsewhere than in the transactions of the society, the co-authorship must be indicated.

The executive session will be held Monday evening, May 31, 1943.

Association for Research in Ophthalmology.—The annual meeting will be discontinued in accordance with the present policy of the American Medical Association. The association will resume its meetings when the next session of the American Medical Association is held. The annual dues will not be collected until the activities of the association are resumed. These decisions have been made by a majority vote of the Board of Trustees.

The Board of Trustees voted the prize award of $100 for the outstanding paper presented at the 1941 meeting to Dr. P. J. Leinfelder and Dr. Nelson M. Black Jr. The title of the paper is "Experimental Transplantation of the Extraocular Muscles in Monkeys."

Florida Council for the Blind.—At a recent meeting in Tampa, Fla., the advisory committee voted to give their services without remuneration for the duration of the war or until such time as a single con-

sulting ophthalmologist can be employed by the council, and they agreed to invite other ophthalmologists to advise and assist the council on a volunteer basis. It was also agreed that the members of the state medical and dental associations be requested to provide general physical and dental examinations for the blind without charge, the council to assume responsibility for payment of the cost of material used. It was further decided to divide the state into three sections, the members to assume responsibility for expansion of the medical features of the sight conservation program in their respective districts. Plans were also formulated to obtain ophthalmic examinations and corrective medical or surgical treatment for the needy residents of the state.

PERSONAL NEWS

Dr. Louis A. Julianelle Appointed to New York Institute.—Louis A. Julianelle, Ph.D., associate professor of applied bacteriology and immunology in ophthalmology, Washington University School of Medicine, St. Louis, and chairman of the trachoma commission there, has been appointed chief of the division of infectious diseases of the Public Health Research Institute of the City of New York, Inc. Dr. Julianelle received his doctor of philosophy degree at the University of Pennsylvania, Philadelphia, in 1922. He served there as instructor in bacteriology until 1924, when he joined the staff of the Hospital of the Rockefeller Institute for Medical Research, New York, as assistant. Later he served as bacteriologist and associate there, joining the Washington University faculty in 1930.

Obituaries

ALLEN GREENWOOD, M.D.
1866–1942

In the death of Allen Greenwood, of Boston, Oct. 23, 1942, aged 76, the world has lost a very useful ophthalmologist. As one follows the simple story of his life, one sees that service was its keynote. His military services were outstanding.

Born in Chelsea, Mass., March 1, 1866, he soon moved to Waltham, where he attended the public schools through high school. He spent three years at Harvard Medical School, graduating in 1889. As was the custom then, he began his hospital service during his last year in the medical school by serving as extern at the Boston City Hospital. His chiefs were Prof. Henry Williams and Dr. Oliver Wadsworth. Since he served under two such masters, it is not surprising that Dr. Greenwood found himself deeply interested in ophthalmology.

On finishing his internship, he took up general practice in his home town of Waltham. Soon he was city health officer (bacteriologist of the board of health). He was also on the surgical staff of the Waltham Hospital.

While carrying on a general practice, he paid special attention to ophthalmology. A few years later he opened an office in Boston for ophthalmic practice, at the same time joining the staff of the Boston City Hospital, with which he had a long and important affiliation.

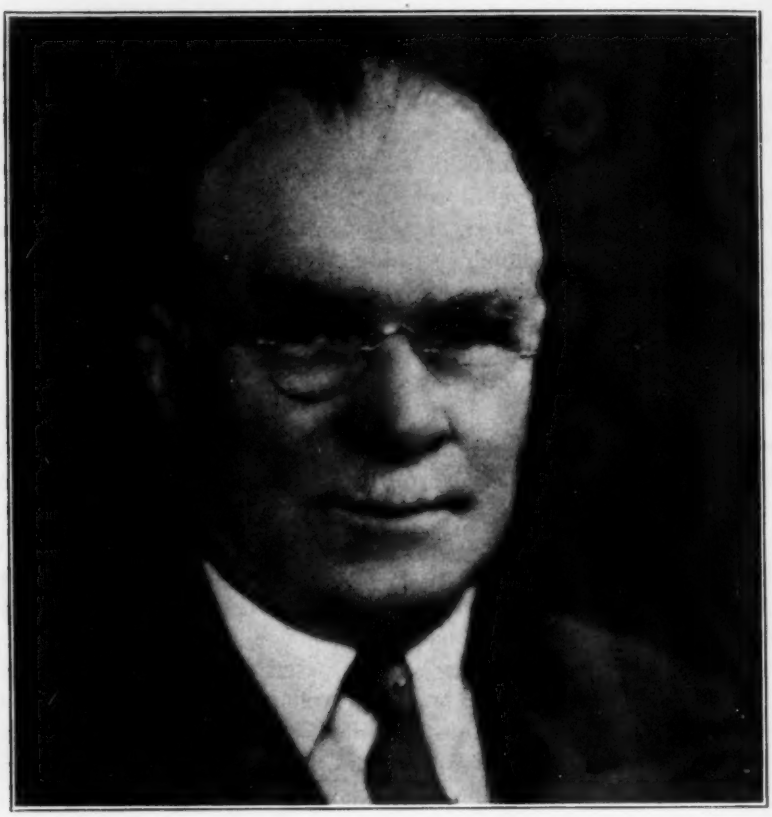
It was during this first decade of his practice that war was declared on Spain. Dr. Greenwood promptly volunteered his services. In Puerto Rico, he had a large hospital filled with soldiers, most of whom had typhoid fever or malaria. He was the sole medical officer for a considerable area of the island besides.

In 1901 I was forced by ill health to give up my practice, which I turned over to Dr. Greenwood. He soon gave up his general practice and moved his residence to Wellesley. Then followed a period of active practice and teaching with some writing.

When Germany started World War I, Greenwood did not wait until the United States declared war but volunteered for one of the hospital units made up in this country for service in France. When the United States became involved, Greenwood rendered invaluable service in the surgeon general's office as personnel officer.

After establishing this fundamental work, Dr. Greenwood was sent to France as senior ophthalmic consultant for the American Expedi-

tionary Forces. Dr. George S. Derby was the other consulting ophthalmic surgeon. This assignment involved visiting all the hospital units, not merely the base hospitals. If, as sometimes happened, he found himself at one of the advanced stations during active fighting, he would lend a hand doing all sorts of emergency operations, often for many hours. He was no narrow specialist.



ALLEN GREENWOOD, M.D.
1866-1942

There were many hardships which he did not spare himself: traveling on crowded trains, sleeping on the floor, irregular meals and very irregular hours. By the time the armistice came, Greenwood was a sick man. In recognition of his services to his country, he received General Pershing's citation for "Exceptionally meritorious and conspicuous services."

When he resumed practice in Boston, it was proposed that he be invited to join the active staff of the Massachusetts Eye and Ear Infirmary, with which he had never been connected. His physician vetoed this, and Dr. Greenwood was made a consultant at the infirmary and at the Massachusetts General Hospital, positions which carried with them the privilege of having private patients at those institutions.

He was professor of ophthalmology at Tufts College Medical School, which trained a larger number of physicians than Harvard. Dr. Greenwood taught also in the Harvard Graduate School of Medicine and as a lecturer in ophthalmology gave a famous course in ophthalmoscopy.

Dr. Greenwood fully appreciated the important part played by medical societies and their value to the practitioner. He was president of the American Academy of Ophthalmology and Otolaryngology in 1918; liaison officer (the most important officer) of the newly formed honor section of the Academy; chairman of the Section on Ophthalmology of the American Medical Association in 1919; president of the American Ophthalmological Society in 1941 and previously chairman of the Council; president of the New England Ophthalmological Society and influential in guiding its activities, especially when any problems were encountered requiring experience and sound judgment. In fact, it was Dr. Greenwood's soundness of judgment that made him so much sought as a consultant. He exemplified Osler's dictum "The value of experience is not in seeing much but in seeing wisely."

Dr. Greenwood contributed much to the American Board of Ophthalmology, which he joined as early as 1916. His special work was on the case reports, of which each candidate presents ten. The labor of reading and evaluating five hundred to a thousand case reports, some of which might be ten pages long, when fifty to a hundred candidates were to be examined, is readily seen. He loved his work, but "It is not true that love makes all things easy—it makes one choose that which is difficult."

Dr. Greenwood was a particularly good operator, combining skilful fingers with resourceful but conservative judgment. One of his contributions in teaching operative surgery, which he did for a good many years, was his custom at the end of each course of having a heart to heart talk with those pupils who showed that they would never make good operators, advising them of the fact and advising them not to undertake major surgical procedures but pass them on to better qualified colleagues.

In discussing the preparation of a physician for ophthalmic practice, he said that he had himself been definitely handicapped by not having a college education. In his day a majority did not. On the other hand, he was a strong believer in and advocate of the advantage of gaining

experience in general practice before specializing in ophthalmology. In this opinion a majority of the men of his day concurred. They knew how the experience has profited them.

A list of papers published by Dr. Greenwood comprises twenty or more items. It gives an inadequate idea of his contributions, because his discussions of papers by other men, based on his wide experience and sound judgment, were bright spots in many a medical meeting.

WALTER B. LANCASTER,
520 Commonwealth Avenue, Boston.

WILLIAM TOY SHOEMAKER, M.D.

1869–1942

William Toy Shoemaker was born in Philadelphia Jan. 22, 1869, the son of Julien Shoemaker, of Plymouth Meeting, Pa., and Hannah Ann Hester Shoemaker, of Trenton, N. J. His preliminary education was obtained in the public schools of Philadelphia. He was graduated from the Central High School, and he received the degree of Doctor of Medicine from the University of Pennsylvania School of Medicine in 1891. He interned at the German Hospital, now the Lankenau Hospital, in Philadelphia. Later he studied ophthalmology in Göttingen, Heidelberg, Berlin, Vienna and London. On his return to Philadelphia, he began the practice of ophthalmology. At various times he was surgeon to the Pennsylvania, Germantown, Lankenau and University of Pennsylvania graduate hospitals; professor of ophthalmology and vice dean of the group in ophthalmology of the Graduate School of Medicine of the University of Pennsylvania; clinical professor of ophthalmology at the Woman's Medical College of Pennsylvania, and executive medical officer of the Lankenau Hospital.

He was a fellow of the American Medical Association, a member of his state and county medical societies, a member of the Association for Research in Ophthalmology, a fellow of the American Ophthalmological Society, a fellow of the College of Surgeons, a fellow of the College of Physicians of Philadelphia and one time chairman of its Section on Ophthalmology. His term of office as chairman was interrupted by his army medical service abroad in World War I.

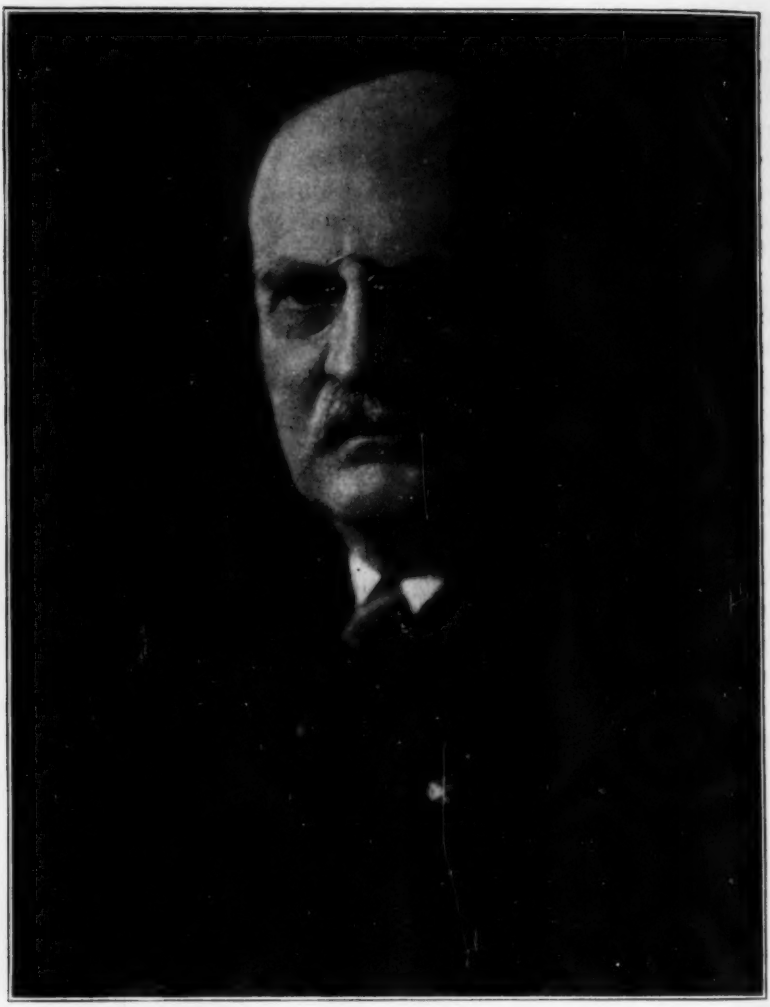
During that war he served as major in the United States Army with Pennsylvania Base Hospital No. 10, which took over British No. 16 General Hospital, B. E. F., La Treport, France. Later he was consultant ophthalmologist at Base Section No. 3, in London, A. E. F. He was overseas nineteen months.

He received the Alverenga award from the College of Physicians of Philadelphia for his essay on "Retinitis Pigmentosa." He contributed chapters on various ophthalmologic subjects in textbooks, encyclopedias and journals. He was for a time editor of the *Annals of Ophthalmology*.

His fraternity was Alpha Mu Pi Omega (medical). He was a member of the Union League, the Military Order of Foreign Wars and the Military Order of World War I.

Read before the Section on Ophthalmology of the College of Physicians of Philadelphia, Dec. 17, 1942.

On June 6, 1895 he married Miss Mabel Warren, of Boston. They had six children, four sons and two daughters. He is survived by two daughters, Mrs. David C. Cleland and Mrs. Albert Zimmermann, and by



WILLIAM TOY SHOEMAKER, M.D.
1869–1942

three sons: J. Warren, of Winchester, Mass.; Theodore, of Lexington, Mass., and Robert C., of Portland, Ore.

Dr. Shoemaker was a keen clinician and an excellent clinical teacher. His surgical judgment was sound, he was eminently practical and his

technic was original, as evidenced by his well known and widely adopted modification of the Motais operation for ptosis.

He was slow to discard the teaching of the early masters and looked somewhat askance at the importance attached to experimental research, evidently believing, with Priestley Smith, that too much credence should not be given to theories based on experimental data when they are at variance with those based on clinical and pathologic observations.

His contributions to the literature were not numerous, because he would not write unless he had something original to communicate. He adopted the same principle in scientific gatherings, so that he never discussed a paper unless he could add something of value to the subject presented.

His writings contain many unique descriptive phrases, and doubtless he had often to restrain his rather sharp wit, which was so characteristic of his comments when he was conversing with an intimate friend.

As an editor, he was discerning in his selection of articles for publication and, at times, aroused criticism from an author by the free use of an editor's prerogative. His book reviews were far from perfunctory, and were at times diverting.

His executive ability was attested by his appointment as executive medical officer of a general hospital and as the vice dean of a medical school.

Dr. Shoemaker's life was rich in friendships, and he had the devotion of his family, the respect and esteem of his colleagues and students and the loyalty of his patients. He was kindly and friendly but reserved.

In his later years, if in a pensive mood he could recall a life of accomplishments, of achievements and of happiness.

W. ZENTMAYER.

SAMUEL POINDEXTER OAST JR., M.D.
1886-1942

Samuel Poindexter Oast Jr. was born on Nov. 27, 1886 at Portsmouth, Va., and on Oct. 16, 1942, at his birthplace, he died. He came of old English stock, long settled in the Tidewater belt of Virginia. He received his premedical education at the Virginia Polytechnic Institute and at the University of Virginia. In 1911 he was graduated from the University of Pennsylvania School of Medicine.

After a period of general hospital preparation and general practice Dr. Oast in 1916 enlisted as first lieutenant in the Medical Reserve Corps of the United States Army. His first active service was with the ambulance corps of the American Hospital of Paris. Later he was transferred to the American Expeditionary Force, with which he participated in the battles of St. Mihiel and Argonne Forest. From Dec. 20, 1918 to Aug. 15, 1919 he was stationed with the Amercian Army of Occupation at Coblenz, Germany. He was discharged from service at Camp Lee, Va., on Sept. 17, 1919.

In 1920 he received an appointment on the house staff of the New York Eye and Ear Infirmary, serving until 1923, first in the aural and later in the ophthalmic department.

In 1925 Dr. Oast was appointed assistant surgeon at the infirmary, and in 1937 he became a full surgeon with a clinic of his own. In 1941 he was made honorary surgeon, which position he filled until his death. In all, through a period of twenty-two years, he rendered faithful and valuable service to the infirmary, to which he was deeply attached as his surgical home. He was an excellent surgeon and a keen clinician, held in the highest respect by his professional associates and all others.

Dr. Oast was a member of a number of medical organizations, among which were the American Medical Association, the American Ophthalmological Society, the American Academy of Ophthalmology and Otolaryngology, the New York Academy of Medicine and the New York Ophthalmological Society. He was a fellow of the American College of Surgeons.

He was not a prolific writer. However, whenever he contributed a paper it was sure to be well done, concise and most informative. He

possessed a genial disposition and was never happier than when entertaining friends at his home. He was fond of outdoor sports, especially tennis and fishing.

Surviving Dr. Oast are his wife, the former Miss Dorothy Frances Harper, of Canada; their sons, Samuel Poindexter Oast 3d and Robert Waring; his aged parents; one sister, and six brothers. His father outlived him only ten days. Of his brothers, three are lawyers and three are physicians—an unusual record for one family.

His passing is greatly lamented by his colleagues and friends.

CLYDE E. MCDANNALD.

Correspondence

CHANGES OF AXIS OF ASTIGMATISM

To the Editor:—In the informative paper "Change of Axis of Astigmatism on Accommodation," by Wendell Hughes (ARCH. OPHTH. **26:** 742 [Nov.] 1941), the author stated that he had been unable to find reports in the literature concerning cases in which the axis of astigmatism accepted by the patient at the near point was different from that acceptable at the far point!

Now, generations of students who have learned the principles of the outmoded optometers (Badal, Young, etc.) have been well aware that such a difference in axis for near and for far vision may occur. In relation to astigmatism itself it is certainly known that (1) in a strong correction the same cylinder will not serve in power for near and for far vision; (2) a cylinder correction for near vision is an overcorrection for distance; (3) any cylinder at a given point from the eye has more corrective power of astigmatism if convex and, conversely, less corrective power if concave; (4) any given amount of cylindric power in the principal plane needs a weaker plus cylinder and a stronger minus cylinder when at a distance from the eye; (5) the astigmatic effect of any cylinder differs with the power of the sphere with which it is combined, and (6) the astigmatic effect differs with the proximity of the object. These are elementary theoretic considerations.

Although it has been said that there is no thoroughly reliable astigmatic near point test, yet there are sufficient test cards in use to show that near point testing for astigmatism is reliable in practice, certainly more reliable than "twisting the axis of the cylinder until the patient sees better."

Refractionists in the Middle West, for example, commonly use the Apel card [1] for near point tests. This has a "reduced" Snellen chart for testing the visual acuity before and after the near point correction and devices, such as "reduced" astigmatic dials and cross cylinder grids, for cross cylinder testing (nonfusion binocular finding), for use with the dissociating prism base up or down in testing heterophoria and for checking the astigmatism at the near point to see whether there is any change in the amount of the cylinder or in the axis of the cylinder from the values found in the test of distant vision.

It is my understanding that optometrists of the better grade use this check card (as I have for five years), with the triangle block to line images in making tests for heterophoria and the black square block with the white circle for making "duction" tests (to determine the relative efficiencies of the medial and lateral rectus muscles; i. e., to find the "zone of comfort" with the base-out and base-in prism tests).

1. Near point test card for examination of eyes, copyrighted, 1937, by Dr. A. W. Apel.

There is nothing "new" in this card except to prove that Apel's card was patented by Apel, *inter alia,* "with a reduced astigmatic dial to check the astigmatism at the near point to see if there is any change in the amount or axis from that found in the distance test." [2]

If medical refractionists do not check near point cylindric findings it is high time (as Dr. Hughes shows) that they begin. Also, in keratometry, with errors of over 2.5 D. (note) a clue can often be found to explain alleged "near accommodative fatigue," in that the axis of the cylinder differs at the near point from that found for distant vision.

Finally, the most accurate near point test of astigmatism and axis is in the use of "dynamic" retinoscopy. This test will prove to the skeptics that changes of "axis accommodation" at the near point do occur.

Whether "sectional" accommodation can take place at the near point, resulting in a "physiologic" "twist" of the axis at the near point is mere guess work. The explanation of the facts (that is, that an axis of astigmatism accepted for distance vision may "fog" a patient at near vision) presented by Dr. Hughes in his informative paper is certainly difficult, but to say that is not the same as stating that these facts have been heretofore unknown. They can be found stated in any description of the optometer, and they are well known not only to those who practice dynamic retinoscopy, occasionally or habitually, but to those who use near point test cards of the Apel variety.

"Diploma" students at the Royal London Ophthalmic Hospital (Moorfields) in 1935 constantly sought explanations of these facts. The explanation of the change in axis was unknown; the fact that a change of axis occurred occasionally for near and for far vision decidedly was known.

HUGH O'NEILL, M.D., Santa Ana, Calif.
2122 North Main Street.

2. Apel, A. W.: Personal communication to the author, 1937.

PARALLACTIC ANGLE

To the Editor:—Lieutenant Colonel Byrnes's comments in the December issue of the ARCHIVES on my article on the "Parallactic Angle in Binocular Depth Perception" (ARCH. OPHTH. **28:** 258 [Aug.] 1942) bring to the fore the want of clearcut definitions of some of the terms used. To start from the beginning, just what is meant by "binocular parallax"? If one consults the two leading medical dictionaries one finds the following definitions: Gould's medical dictionary says, "Binocular parallax is the angle of convergence of the visual axes"; Dorland's "American Illustrated Medical Dictionary" says "Binocular parallax is the seeming difference in position of an object as seen separately by one eye and then by the other, the head remaining stationary." Different dictionaries are expected to define the same term in somewhat different ways but to convey the same meaning. These two definitions do not convey the same meaning. Furthermore, the term "binocular parallax" as used by different writers conforms to neither of the two

definitions found in the dictionaries. Similar looseness, though less marked, applies to the terms "binocular stereoscopic parallax," "angle of parallax," "stereoscopic parallax," "angle of stereoscopic parallax," "parallactic angle," "motion parallax," etc. I used the term "binocular parallax" in the sense of the definition in Gould's dictionary. This is how Duke-Elder used it.[1] The "parallactic angle" as I defined the term and used it in my article is identical with the angle which Lieutenant Colonel Byrnes termed "the parallactic angle." The difference pertains merely to the conception of the formation of the angle.

In Lieutenant Colonel Byrnes's diagrams the angles *ARB* and *ALB* are the visual angles subtended by the two points *A* and *B* at *R* and *L*, that is, at the right and the left eye, respectively. Points *A* and *B* may be parts of the same object or separate object points. These angles are taken in a static sense, the eyes being stationary, and the difference between these static visual angles is "the parallactic angle." This is a conception of the "parallactic angle" based on the belief that dissimilarity of retinal images is the sole or principal factor in depth perception. Most authorities adhere to this view. But if the influence of convergence in depth perception is a factor at all, and there are a good many authorities who believe that it is, then it is most likely the dynamic neuromuscular exercise of a change of convergence which is the effective agent. This, of course, involves moving the eyes to change fixation from point *A* to point *B*. The same two angles, *ARB* and *ALB* will then be the angles through which the right and left visual axes turn in order to change fixation from *A* to *B*. They become rotation angles instead of visual angles. The difference between these dynamic angles is what I termed the "parallactic angle" in a dynamic sense. The value of the angle is equal to the difference between the angles of convergence at *A* and *B*, i. e. angles *RAL* and *RBL*. Dr. Howard, in the original description of his test, used the term "binocular parallactic angle" for the difference between the angles of convergence at the nearer and the further rod. But even if the eyes are stationary and the angles at *R* and *L* taken as visual angles, the "parallactic angle" as defined by Lieutenant Colonel Byrnes is still equal to the difference between angles *RAL* and *RBL*.

When the two points *A* and *B* lie on the median line, as in my diagram, view *A*, there will be no disparity of the retinal images. The perception of depth must then be more dependent on the change of convergence. The "parallactic angle" must be taken as the difference between the two angles of convergence in a static sense, or as the difference between the rotation angles of the right and left eye, in a dynamic sense. Duke-Elder[1] used a similar diagram and said: "Stereoscopic acuity is determined . . . by the smallest discernible difference in binocular parallax," and by binocular parallax he apparently meant the angle of convergence at each of the two points.

Lieutenant Colonel Byrnes has given an excellent summary of the various elements involved in binocular depth perception. But the pur-

1. Duke-Elder, W. S.: Text-Book of Ophthalmology, St. Louis, C. V Mosby Company, 1933, vol. 1, p. 1077.

pose of my paper was to touch on only one element and make it more meaningful by analyzing the innervations involved. I do not think that introducing this bit of ocular physiology complicates the subject.

JOSEPH I. PASCAL, M.D., New York.

37 West Ninety-Seventh Street.

OPHTHALMOLOGICAL SOCIETY OF THE UNITED KINGDOM

To the Editor:—At the beginning of the war the Council of the Ophthalmological Society of the United Kingdom decided that all members of the society who joined the forces should be exempted from paying their subscriptions for the duration of the war, while still retaining the full privileges of membership, which include the receipt of all published transactions.

My council would like it to be understood that this ruling includes American members. All that is necessary is that the member concerned should inform the treasurer, Sir Arnold Lawson, 12 Harley Street, London, W. 1., of his having joined the forces, his date of joining, his unit and rank and any change of address to which communications may be sent.

In the event of any subscription having been paid since the member joined the forces, the amount will be refunded.

FRANK W. LAW, M.D., F.R.C.S.
Secretary.

Abstracts from Current Literature

EDITED BY DR. WILLIAM ZENTMAYER

Anatomy and Embryology

TOPOGRAPHY OF FIBERS OF OPTIC NERVE IN RELATION TO RETINAL TERRITORIES. M. BALADO and E. P. FORTIN, An. argent. de oftal. **2:** 135 (July-Sept.) 1941.

The authors have studied the distribution of the fibers of the optic nerve when they penetrate into the scleral foramen to form the disk. They are in agreement with the ideas supported by Fuchs, according to which the fibers coming from the peripheral parts of the retina reach the center of the optic nerve, while those from the retina in the vicinity of the disk enter the nerve near the borders of the scleral foramen. The peripheral fibers are not in the plane of their origins in the ganglion cells when they run to the disk, but are continually pushed up by new fibers starting from the central portions of the retina. In this way is formed, especially at the temporal side of the disk, a semicircular elevation having a nasal concavity, of which the apex is formed by the optic fibers coming from the periphery and the base by the fibers arising from the retina immediately around the disk. By the study of microscopic sections of stained retinas of animals, the authors found that there is no crossing of the fibers at the disk, as described by Michel and Holliker and accepted in the schema of Henschen and von Hippel. In the nasal portion of the disk the same arrangement exists.

Balado and Fortin criticize Henschen's schema of the arrangement of the fibers in the disk. They submit a new one, in which the position of the different bundles of fibers coming from the macula and its vicinity into the disk is well represented.

For a better understanding of this paper the authors' illustration and schemas should be examined in the original.

M. U. TRONCOSO.

Biochemistry

THE PROTEIN CONTENT OF THE AQUEOUS HUMOR IN MAN. P. C. KRONFELD, Am. J. Ophth. **24:** 1121 (Oct.) 1941.

Kronfeld gives the following summary of his findings:

"With a method based on estimation of the turbidity produced in the aqueous humor by the addition of sulphosalicylic acid the protein content of the aqueous humor (p_1) was determined on a large number of patients under varying conditions. It was found that:

"1. No appreciable contamination with re-formed aqueous occurs during careful but complete aspiration of the contents of the anterior chamber.

"2. Repeated p_1 determinations on the same eye showed variations of less than ± 15 per cent of the average.

"3. Equality of p_1 in the two eyes of the same individual seemed to be the rule, inequality the exception.

"4. In four groups of cases—namely, normal controls, cases of retrobulbar neuritis due to dietary deficiency, cases of primary optic atrophy, and cases suspected of representing or proved to represent early stages of primary compensated glaucoma—p_1 varied within the same limits; that is, from 5 to 16 mg. per cent.

"5. This range may be considered the normal range of p_1.

"6. In senile cataract with cortical breakdown p_1 is increased, probably because of diffusion of lens proteins into the anterior chamber.

"7. In the pure, compensated form of primary glaucoma, p_1 is within normal limits."

W. S. REESE.

Conjunctiva

BITÔT'S SPOTS IN TRINIDAD. V. M. METIVIER, Am. J. Ophth. **24:** 1029 (Sept.) 1941.

Metivier discusses Bitôt's spots in relation to xerophthalmia and their occurrence in Trinidad. He concludes that a simple method of assessing the state of nutrition among large groups of children is the incidence of angular stomatitis, phrynoderma and Bitôt's spots.

W. S. REESE.

FOUR UNUSUAL CASES OF CONJUNCTIVITIS. E. F. KING, Brit. J. Ophth. **26:** 467 (Oct.) 1942.

The following clinical features were common to the cases of conjunctivitis observed by King:

On preliminary examination slight ptosis was seen, together with boggy fulness of the skin of both the upper and the lower lid. The eye tended to water and to be photophobic, but, in general, discharge was scanty except during periods of secondary infection. The injection of the conjunctiva was largely confined to the posterior surface of the lids and the fornices, particularly the lower, and to the region of the plica and the caruncle. This distribution of the hyperemia was striking and contrasted markedly with the relative whiteness of the ocular conjunctiva. The whole conjunctiva was somewhat edematous, and there was a diffuse milkiness, particularly in the lower fornix, reminiscent of spring catarrh and presumably the result of epithelial hyperplasia.

In the upper fornix were a few scattered follicles. In the 2 cases of more severe conjunctivitis, subconjunctival fibrosis developed in the lower fornix, and in 1 case it led subsequently to marked contraction.

In 2 cases the cornea remained unaffected. In the other 2 a diffuse superficial keratitis was seen, extending over the greater part of the cornea; superficial vascularization occurred, and the whole picture was similar to diffuse phlyctenular keratitis of childhood.

A striking feature is that the conjunctivitis in each case remained entirely unilateral, there being no suggestion of involvement of the conjunctiva or cornea in the second eye. The condition was persistent and chronic in its course. At the latter part of last year it had lasted in

1 case for eight, in another for seven and in 2 for four months. During these times the patients had been completely incapacitated from their duties and had spent the greater part of the time in the hospital. There was seen during this period intermittent infection with secondary pyogenic organisms accompanied by exacerbation of the keratitis and enlargement of the preauricular gland.

In the 2 cases of severe involvement, in which subconjunctival fibrosis occurred, the patient was invalided out of the Army; in the other 2 the patient ultimately returned to duty, although the condition was still present and further relapses seemed probable. W. ZENTMAYER.

Congenital Anomalies

HEREDITARY PTOSIS AND IMBECILITY. J. TATÁR and Z. VON PAP, Arch. f. Ophth. **142:** 627, 1941.

This report concerns a Hungarian family in which the father, 4 sons and 2 daughters showed the following anomalies: bilateral ptosis, blepharophimosis, underdevelopment of the tarsi, paralysis of the superior rectus muscles and overdevelopment of the eyebrows. One son was an imbecile. P. C. KRONFELD.

Cornea and Sclera

FORMALINIZED HETEROGENEOUS AND HOMOGENEOUS CORNEAL TRANSPLANTATION—EXPERIMENTAL. M. WIENER and H. D. ROSENBAUM, Am. J. Ophth. **24:** 1384 (Dec.) 1941.

With Salzer's work as a foundation, Wiener and Rosenbaum attempted penetrating grafts of corneas fixed with solution of formaldehyde. Twenty-two keratoplasties were done, in 5 of which fixed dog corneas were grafted to rabbits' eyes and in 17 of which fixed rabbit corneas were grafted to rabbits' eyes. W. S. REESE.

A NOTE ON TWO CASES OF MEGALOCORNEA. L. H. SAVIN, Brit. J. Ophth. **26:** 265 (June) 1942.

The first case was that of a man 58 years of age recovering from hemorrhage from a gastric ulcer. There was also severe bleeding from piles. There was bilateral megalocornea. Each iris was somewhat atrophic. The pupils were vertically oval. There was bilateral arcus senilis. The tension was normal. Both lenses showed cuneiform cortical opacities. Later the right eye, which had poor light projection, was operated on. A large conjunctival flap was made, an iridectomy was done and intracapsular extraction was performed. Examination of the fundus showed an atrophic disk and a patch of choroidal atrophy. The left eye was operated on by the same technic. The resulting visual acuity was 6/9.

A grandson had meglacornea with clear lenses and arcus senilis. An uncle also had megalocornea. It will be noted that all 3 patients were males. There was no consanguinity. W. ZENTMAYER.

CONJUNCTIVOPLASTY FOR EXPOSURE KERATITIS. A MIKLÓS, Arch. f. Ophth. **142:** 615, 1941.

To prevent exposure keratitis due to proptosis the author recommends as a routine procedure tenotomy of the levator after the method of von Blaskovics instead of the customary tarsorrhaphy. In a case of severe proptosis, due to toxic goiter, with advanced keratitis the tenotomy of the levator failed to keep the keratitis from progressing. Sympathetic denervation had no effect on the degree of proptosis. Covering of the entire cornea with an apron-shaped conjunctival flap from above resulted in a "cure" within one week. "The pain stopped immediately." The author apparently did not have an opportunity of examining the cornea again or of doing anything further. He believes, however, that "later on the vision can be restored by cutting a small hole in the center of the conjunctival flap" and that "no danger of recurrence of the keratitis is entailed in this procedure."

P. C. KRONFELD.

General Diseases

CEREBRAL SYMPTOMS ACCOMPANIED BY CHOKED OPTIC DISCS IN TYPES OF BLOOD DYSCRASIA. C. H. WATKINS, H. P. WAGENER and R. W. BROWN, Am. J. Ophth. **24:** 1374 (Dec.) 1941.

After a brief discussion and review of the literature, Watkins, Wagener and Brown give the following summary and conclusions:

"Three cases of thrombocytopenic purpura are reported in which bilateral choked optic discs were present in the absence of a demonstrable extraneous intracranial pathologic process or lesion. In none of these cases could it be proved that intra-meningeal or intracerebral bleeding had occurred.

"Another case . . . is reported in which choked optic discs appeared in the course of recurrent severe hemorrhage from a gastric ulcer. In this case an intracranial pathologic process or lesion could not be demonstrated at necropsy. It is suggested that the mechanism of production of papilledema was essentially the same in these four cases: a local reaction of the tissues of the optic nerves to anoxemia that resulted from loss of blood.

"It is concluded that edema of the brain arising from the same cause may be a factor in the development of the papilledema and of the paralysis of the lateral-rectus muscles at times associated in such cases."

W. S. REESE.

THE TOXIC SYNDROME OF OCULAR TUBERCULOSIS. C. CHARLÍN, Am. J. Ophth. **24:** 1392 (Dec.) 1941.

Charlin describes the headaches, anorexia, loss of weight, etc., that accompany ocular tuberculosis as a toxic syndrome. He emphasizes the importance of these symptoms in treatment and reports 4 cases.

W. S. REESE.

General Pathology

OCCURRENCE OF BLOOD VESSELS IN INTERLAMELLAR LAYER OF UVEA NEAR ORA SERRATA. J. MELLER, Arch. f. Ophth. **142:** 507, 1941.

In two recent papers (Reichling, W., and Klemens, F.: *Arch. f. Ophth.* **137:** 515, 1937; **141:** 500, 1940), Reichling and Klemens claimed to have found a vessel-carrying connective tissue layer between the retinal pigment epithelium and the lamina vitrea in normal eyes. They stated, "It is surprising that the vascular layer between the pigment epithelium and the lamina vitrea and its precursors has never been noticed or recorded."

Meller takes issue with this statement. After describing and discussing in detail pertinent sections from his own histologic collection, he sums up as follows: It has been known for a long time that blood vessels can occasionally be seen in the extremely narrow space between the two lamellas of the lamina vitrea, the basal membrane of the pigment epithelium, on the one hand, and the elastic lamella of the choroid, on the other hand. Near the ora serrata these two lamellas are clearly separated by collagenous connective tissue fibers. Vessels present in this space are not necessarily or always the result of an inflammatory process but may represent remnants of fetal tissue. During early fetal life the elastic lamella near the ora is not a single continuous membrane. Thus it is possible that intrachoroidal vascular loops which originally extended up to the basal membrane remain there all through extrauterine life. Salzmann noted such vessels and considered them to be abnormal. Meller believes, however, that most of the blood vessels which are found in the interlamellar space are vessels embedded in newly formed, postinflammatory connective tissue. Thus blood vessels in the interlamellar space are a common occurrence in eyes with various forms of uveitis and with newly formed membranes in other portions. In eyes without gross evidence of uveitis, painstaking examination practically always reveals the association of blood vessels in the interlamellar space with histologic signs of healed localized uveitis, so that "there is hardly a case left in which one could detect the presence of vessels in the interlamellar space in the choroid of a normal eye."

As the most significant result of his study, Meller considers recognition of the fact that inflammation of the anterior portion of the uvea leads more often than is generally believed to exudation into and formation of connective tissue within the interlamellar space without the formation of any such tissue on the inner surface of the choroid. An exudate formed farther back in the choroid, where there is no interlamellar space, is forced out of the choroid into the space between the retina proper and the pigment epithelium, where it gives rise to the usual chorioretinitic adhesions and membranes. Thus, interlamellar connective tissue with blood vessels is the typical result of an inflammatory process near the ora serrata.

P. C. KRONFELD.

Glaucoma

GONIOSCOPIC OBSERVATIONS IN CYCLODIALYSIS OPERATIONS. S. T. CLARKE, Am. J. Ophth. **24:** 1026 (Sept.) 1941.

Clarke observed 34 cases of cyclodialysis clinically and gonioscopically as to efficacy and indications for this operation. His findings bear

out Barkan's report as to the mode of action of cyclodialysis and the gonioscopic findings in cases of successful and of unsuccessful operation.

W. S. REESE.

GLAUCOMA ASSOCIATED WITH HYALINE BODIES (DRUSEN) OF THE OPTIC DISC. A. G. ATHENS, Am. J. Ophth. **24:** 1138 (Oct.) 1941.

Athens briefly reviews the conditions coexisting with drusen and reports the case of a 19 year old girl with bilateral drusen of each nerve head, the eye with the more pronounced drusen also having glaucoma. He speculates as to a relationship between these two conditions.

W. S. REESE.

VALUE OF GONIOSCOPY IN THE PROGNOSIS AND TREATMENT OF GLAUCOMA. M. U. TRONCOSO, Am. J. Ophth. **24:** 1396 (Dec.) 1941.

Troncoso gives the following summary of his observations:

"A new model of gonioscope is described, which has no prisms and gives a direct lateral view of the angle with good magnifications (10 × and 20 ×). The instrument carries its own illuminating system, is monocular, and as easy to handle as the ordinary ophthalmoscope. It may be made binocular if so desired.

"Gonioscopy shows the development of the characteristic symptom of glaucoma in the angle of the anterior chamber; namely, anterior peripheral synechia. The author studies its frequency in the different types of the disease and its importance on the prognosis and treatment. In congestive glaucoma the prognosis improves when an early iridectomy is performed. The fellow eye should be carefully examined.

"In chronic simple glaucoma gonioscopy gives important data which should be added to the other well-known symptoms of hypertension. The old idea of continued treatment with miotics alone should be revised. If slight attacks of hypertension appear, if changes in the field of vision advance, and a peripheral synechia begins to form in one or several sides of the limbus, it is time for an operation. In a general way, an early operation gives a better prognosis in primary glaucoma.

"In the treatment of glaucoma, gonioscopy is important before and after operations. Iridectomy, cyclodialysis, trephining, iridencleisis, and other operations have more chance of success when performed at places where the angle is open. The Lagrange operation or trephining opens a permanent channel of outflow, but the second is usually followed by complications. Cyclodialysis may be useful even when there is a peripheral synechia."

W. S. REESE.

Hygiene, Sociology, Education and History

WOLLASTON AND HEMIANOPSIA. J. E. LEBENSOHN, Am. J. Ophth. **24:** 1053 (Sept.) 1941.

Lebensohn briefly reviews Wollaston's research, his description of hemianopsia (the first recorded), from which he himself suffered, and the story of how he developed the theory of semidecussation of the

optic nerves. Wollaston finally died from a brain tumor, to the last directing his research and observations on himself. His intellect, as he demonstrated, remained unclouded to the end, in spite of extensive cerebral disease, shown by autopsy. W. S. REESE.

Injuries

SCLERO-KERATITIS FOLLOWING PHOSPHORUS INJURY OF THE EYE. T. K. LYLE and A. G. CROSS, Brit. J. Ophth. **26:** 301 (July) 1942.

The authors were unable to find in the literature a case of phosphorus injury to the eyes. Their patient was an airman. The injury occurred in April 1918, resulting from the explosion of a barrel of phosphorus during its removal from a water storage tank. The lesion resembled mustard gas keratitis in recurrences of the inflammation separated by long intervals. The main lesion was scleritis, with corneal scars deep in the substantia propria, differing from the usual type of sclerokeratitis, in which the corneal opacity is in continuity with the sclera and in which uveitis is present. The state of the cornea indicated a degenerative condition, and it is suggested that this originated when the eyes were injured with phosphorus twenty-four years ago. W. ZENTMAYER.

Lens

BARRAQUER'S PHACOERESIS WITH CORNEAL SUTURE. J. MALBRÁN, Arch. de oftal. de Buenos Aires **16:** 572 (Oct.) 1941.

Malbrán presents a new series of 50 cases in which the operation was supplemented by a corneal suture. He reviews the different varieties of sutures, from which he selects the Leech and Sugar variation of the Stallard suture.

The operative complications were greatly reduced. The visual results are not reported.

C. E. FINLAY.

REMARKS ON ORIGIN OF SENILE CATARACT AND SOME OTHER FORMS OF CATARACT. C. LINDAHL, Upsala läkaref. förh. **47:** 107 (Oct. 5) 1941.

Lindahl discusses the genesis of various kinds of cataract—diabetic, tetanic, dinitrophenol, syndermatotic and myotonic, as well as senile cataract, which is generally considered a separate form. They are all almost always bilateral, and associated with them is an abnormal state of nutrition expressed by an abnormal composition of the blood. Senile cataract is regarded as associated with a deficiency in the blood of substances necessary for the metabolism of the lens. The change in composition of the blood leads to a change in the aqueous humor, resulting in a disturbance of the metabolism of the lens and the origin of bilateral cataract. Statistics show the number of patients treated for cataract to be relatively higher during periods of high prices and consequent deficiencies in diet, especially in vitamin C and glutathione.

J. A. M. A.

Methods of Examination

AUTOFUNDOSCOPY. L. C. DREWS, Am. J. Ophth. **24:** 1403 (Dec.) 1941.

Drews discusses the various aspects of autofundoscopy and arrives at the following conclusion:

"1. Autofundoscopy properly used and interpreted is of great clinical value.

"2. In central retinal lesions autofundoscopy combined with visualization of afterimages of crossed filaments of light is of practical value in measuring the central lesion, and is as accurate as the patient's sense of proportion. Apparently priority may be claimed for this procedure.

"3. The afterimages of one eye may be used to measure a central retinal lesion and to locate the foveal area of the other eye. Apparently, priority may be claimed for this procedure, also.

"4. Retinal detachment is one condition in which autofundoscopy may be entirely unreliable.

"5. Pure choroidal lesions and lesions localized strictly to the inner layers of the retina are easily differentiated, if centrally located.

"6. The central and paracentral areas are very easy to investigate. No claim is made that lesions outside the central 10 degrees of the retina may be reliably investigated in the average patient by this method. No claim is made that autofundoscopy replaces quantitative central-field studies. . . .

"7. Accentuation of the afterimage with autofundoscopy may be considered as an induced afterimage effect. Such accentuation has not, to the writer's knowledge, been described before.

"8. A unique foveal lesion is described. . . .

"9. The scotoma of the optic-nerve head appears very much smaller with autofundoscopy than it actually is. This is of fundamental physiological importance.

"10. An immense amount of work remains to be done on this subject."

W. S. REESE.

Neurology

OCULOGYRIC CRISES. R. M. KLEMME, Am. J. Ophth. **24:** 1000 (Sept.) 1941.

In the course of operations on patients with paralysis agitans and athetosis of postencephalitic origin, Klemme found that 3 of those with oculogyric crises had no further crises. He then operated successfully on a patient with oculogyric crises. He reports on this patient and presents the following conclusion:

"Operative interference with removal of premotor cortex at the junction of the first and second frontal convolutions adjacent to the anterior edge of the motor cortex is the treatment of choice in patients with oculogyric crises."

W. S. REESE.

MULTIPLE SCLEROSIS IN THE AMERICAN NEGRO. L. C. KOLB, Arch. Neurol. & Psychiat. **47:** 413 (March) 1942.

The authors considered as definite cases of multiple sclerosis only those in which a predominant number of the following criteria were satisfied: onset of symptoms between the ages of 15 and 55, a history of remissions and exacerbations of the disease, subjective or objective sensory disturbances, objective evidence of disease of the pyramidal tract or cerebellum, nystagmus, slurred speech, loss of the abdominal reflexes, retrobulbar neuritis, presence of central scotomas, pallor of the optic disks and changes in the cerebrospinal fluid. They found that Negroes in Baltimore are as subject to multiple sclerosis as the native and the foreign-born white population. The clinical features of the disease in the Negro are similar to those seen in the white man. The disease in the Negro is often mistaken for syphilis and in some instances occurs with syphilis in the same person.

R. IRVINE.

Ocular Muscles

EXPERIMENTAL TRANSPOSITION OF THE EXTRAOCULAR MUSCLES IN MONKEYS. P. J. LEINFELDER and N. M. BLACK JR., Am. J. Ophth. **24:** 1115 (Oct.) 1941.

Leinfelder and Black found, after transposing the tendons of the medial and the inferior rectus muscle of monkeys, that there was complete return of coordinated rotations. In a second group of animals, in which, in addition, the superior and the lateral rectus muscle were transposed, coordinated rotations returned but there was some disturbance in the extent and the type of ocular movements. In a third group the four rectus muscles were transposed as before and the tendon of the superior oblique muscle resected. In these animals there was no return of coordinated rotations. The experiments demonstrated that absence of vision had no appreciable effect on the outcome.

W. S. REESE.

ORTHOPTIC TRAINING AND THE SURGICAL CORRECTION OF STRABISMUS. C. BERENS, A. J. ELLIOT and L. SOBACKE, Am. J. Ophth. **24:** 1418 (Dec.) 1941.

From an analysis of the histories of 324 patients with strabismus operated on at the New York Eye and Ear Infirmary, Berens, Elliot and Sobacke conclude that orthoptic training is an indispensable adjunct to the surgical treatment of strabismus.

W. S. REESE.

INVOLUNTARY CONVERGENCE, EYESTRAIN AND SQUINT. N. A. STUTTERHEIM, Brit. J. Ophth. **26:** 216 (May) 1942.

This paper is in part controversial and largely an enthusiastic endorsement of the "kinetic" treatment of eyestrain, predicated on the assumption that "in convergence lies the main solution of the great problem of eyestrain."

W. ZENTMAYER.

Operations

CAPSULOTOMY AND IRIDOCAPSULOTOMY. C. BERENS, Am. J. Ophth. **24:** 915 (Aug.) 1941.

Berens describes his technic of capsulotomy and iridocapsulotomy with a special keratome and iridocapsulotomy scissors. He gives the following summary and conclusions:

"The successful production of an artificial pupil often means restoration of vision to a patient who otherwise would be blind. For this reason every effort should be made to avoid serious complications. The opinion is expressed that all but the finest capsular membranes should be cut with scissors because of the great danger of traction on the ciliary region with resulting iridocyclitis and possibly detachment of the retina. A sharp hollow-ground narrow keratome is used to penetrate the sclera subconjunctivally and to perforate the iris and capsule. The incision in the iris and capsule is made with iridocapsulotomy scissors (modified Noyes) which fill the scleral opening and are easy to manipulate. The position of the incision in various conditions, which have been encountered, is described and illustrated."

W. S. REESE.

Orbit, Eyeball and Accessory Sinuses

HEREDITARY CRANIOFACIAL DYSOSTOSIS. E. A. VORISEK, Am. J. Ophth. **24:** 1014 (Sept.) 1941.

Vorisek reports 2 cases of hereditary dysostosis craniofacialis and gives the following summary:

"Two typical cases of Crouzon's disease without hereditary implications are reported. One boy, who was observed for 5½ years, had decompressions of both cranium and orbit with unexpected success. The other boy, observed for only 2½ years, most probably should have decompressions at an early date."

W. S. REESE.

EXOPHTHALMOS. E. E. COVITZ, Am. J. Ophth. **24:** 1423 (Dec.) 1941.

Covitz discusses exophthalmos as the first manifestation of thyrotoxicosis. He gives the following summary and conclusions:

"Three cases are presented and described in which the first or only complaint was exophthalmos. The condition progressed in spite of continued negative signs and symptoms. The diagnosis of Graves's disease was made in each case after an interval of 20 months, 6 months, and 8 months, respectively.

"An interesting sidelight in this presentation was the fact that two of the patients were brothers, which suggests the importance of heredity in Graves's disease.

"In the differential diagnosis of exophthalmos, when the physical, chemical, and x-ray examinations and determinations are negative, exploratory operation of the orbit for tumor should be delayed until Graves's disease is definitely excluded."

W. S. REESE.

Pharmacology

PENETRATION AND DISTRIBUTION OF SODIUM SULPHACETAMIDE IN OCULAR TISSUES OF RABBITS. J. M. ROBSON and W. TEBRICH, Brit. M. J. **1:** 687 (June 6) 1942.

To determine the most suitable concentration and frequency of administration of sodium sulfacetimide under clinical conditions, the authors made the following experiments: Solutions of this remedy were applied to the eyes of rabbits, contact was maintained for various periods of time and the penetration of the drug into the various ocular tissues was then determined. The rate of disappearance of the drug introduced into the eye was also studied. Drops of a 2.5 or 30 per cent solution of sodium sulfacetimide were instilled into the conjunctival sac, and the concentration of the drug in the ocular tissues at various periods after the instillation was determined. When a 2.5 solution was used, chemotherapeutic levels were observed only in the conjunctiva. The advantages of the local application of the sulfonamide compounds in the treatment of ocular infections are discussed.

ARNOLD KNAPP.

Retina and Optic Nerve

MARBLE BONES AND OPTIC ATROPHY. R. O. RISER, Am. J. Ophth. **24:** 874 (Aug.) 1941.

Riser gives a short history of Albers-Schönberg disease and reports a case, commenting that his is the first discussion of the disease from an ophthalmologic viewpoint. He gives the following summary:

"1. Optic atrophy and associated ocular findings are very commonly found in infants and children with osteopetrosis.

"2. Optic atrophy is not a feature of adult osteosclerosis.

"3. An ophthalmologist, confronted by a young patient with optic atrophy and negative Wassermann test, may well advise roentgenological studies of the child's bones, for he might be dealing with a case of Albers-Schönberg's disease."

W. S. REESE.

THE RETINA AND INTRAOCULAR TENSION DURING PROLONGED INSULIN COMA. A. GRALNICK, Am. J. Ophth. **24:** 1174 (Oct.) 1941.

Gralnick reports the case of a 40 year old woman who had an irreversible coma after insulin therapy for paranoid dementia praecox and died. The postmortem observations are given, and the following conclusions presented:

"In prolonged insulin coma of 10 days' duration: (1) The retina appeared to escape damage although the brain sustained extensive injury. (2) The ophthalmoscope revealed no gross pathology. This finding supports one made in a previous paper that the fundi are negative in patients with functional psychoses given routine insulin-shock therapy. (3) The intraocular tension remained uniformly low, and fluctuated inexactly with the spinal pressure. (4) The intraocular tension had no relation to the blood pressure or blood- and spinal-sugar

levels. (5) The finding of lowered intraocular tension corresponds to that of most investigators who report the same in routine insulin comas of short duration."

W. S. REESE.

Tumors

TUMORS OF THE OPTIC NERVE. J. P. GOMES, Am. J. Ophth. **24:** 1144 (Oct.) 1941.

Gomes reports 13 cases of tumor of the optic nerve. He discusses the diagnosis, degree of malignancy, clinical and histopathologic classification, relation between tumors of the optic nerve and von Recklinghausen's disease and methods of surgical treatment. W. S. REESE.

COMPARATIVE STUDIES ON "PHAKOMAS" OF THE EYEBALL AND ITS ADNEXA: REPORT OF CASES. C. PASCHEFF, Klin. Monatsbl. f. Augenh. **104:** 595 (May) 1940.

Congenital spots occur on the eyes which are similar in development to nevi of the lids and conjunctiva but which contain no nevus cells. Pascheff accepts Van der Hoeve's terms "phakoma" and "phakomata." He classifies the spots into four groups: (1) phakoma palpebrae, to which belong naevus flammeus with infantile glaucoma, neurofibroma plexiforme palpebrae with infantile glaucoma, elephantiasis neurofibromatosa palpebrae and congenital posterior cortical cataract; (2) phakoma iridis and glaucoma simplex; (3) phakoma retinae, with the subdivisions phakoma retinae of Recklinghausen's disease and phakoma iridis of Bourneville's disease, and (4) phakoma nervi optici, including primary tumors of the optic nerve, which are rare, and angiofibromatous or pigmented meningoblastomas of the optic nerve. The various types are illustrated with about twenty-five photographs, some of them photomicrographs.

The author concludes that these tumors are not malign but are apt to cause changes in the adjoining bones and damage to vision. The tumors may be classified, according to their location, as phakomas of the lids, iris, retina and optic nerve. Phakomas of the lids (neurofibroma and naevus flammeus) may be accompanied by infantile glaucoma, astigmatism, cataract and amblyopia. These forms are congenital, the same as the tumor (phakoblastoma) itself. Phakomas of the iris are usually combined with glaucoma, according to Pascheff's observation.

Phakomas of the retina are rare and are coupled with phakomas of the skin (Recklinghausen's, Bourneville's and Sturge-Weber's disease). Phakomas of the optic nerve are very rare; Pascheff observed only 2 cases in forty years. Primary congenital tumors of the optic nerve occur which do not originate from Schwann's sheaths of the optic nerve, as they are absent in the fibers of the optic nerve. The two forms of tumors of this group mentioned may cause choked disk through adhesions to the optic nerve, or they may proliferate far into the orbit, leading to amaurosis. Amaurosis occurred in 1 of Pascheff's cases; no recurrence or cerebral lesion developed during eight years of postoperative observation.

K. L. STOLL.

Vision

CAN PRESENCE OF NIGHT BLINDNESS BE PROVED WITH CERTAINTY IN A CASE OF DOUBT? REPORT OF CASES. W. KYRIELEIS, Klin. Monatsbl. f. Augenh. **104:** 663 (June) 1940.

Requirements of the soldier at the front and of the civilian during black-outs have shown the importance of paying attention to night blindness, commonly an irrelevant disturbance. Exact examination is essential but difficult owing to the variation in adaptation of the same person at different times and to malingering. The author found a method by which he could prove an individual constancy in adaptation (see also Kyrieleis, W.: *Arch. f. Ophth.* **138:** 564, 1938). He uses Comberg's adaptometer, described and illustrated in "Kurzes Handbuch" (Schieck, F., and Brückner, O.: Kurzes Handbuch der Ophthalmologie, Berlin, Julius Springer, 1931). Repeated examinations under exactly the same conditions render it impossible for a malingerer to remember detail. Night blindness is present if approximately the same data for the curve of adaptation are obtained at several tests.

K. L. STOLL.

Vitreous

EXPERIMENTAL STUDIES ON VITREOUS DETACHMENT. L. VON SALLMANN, Am. J. Ophth. **24:** 1349 (Dec.) 1941.

Von Sallmann gives the following summary of his experiments:

"1. The effects of osmosis, dehydration, discharge, and pressure on volume decrease and the basic reversibility of the loss were demonstrated in experiments on the vitreous *in vitro* and in some experiments *in vivo*.

"2. No conclusive results of the effect of enzymes (proteases, hyaluronidase) were observed *in vitro* or *in vivo*.

"3. In contrast to the volume increase of protected-vitreous preparations in 0.9 per cent sodium chloride, a loss in volume was obtained by damaging the posterior pole of the preparation.

"4. The results with damaged-vitreous preparations support the theory that a vitreous detachment may be caused by degenerative changes in the area martegiani."

W. S. REESE.

Sympathetic Ophthalmia

A CASE OF SYMPATHETIC OPHTHALMIA FOLLOWING SCLERAL RUPTURE. G. PFEIFFER, Arch. f. Ophth. **142:** 592, 1941.

The case was that of a cow horn injury to the right eye of a farmer 45 years of age. Seven weeks after the injury corneal precipitates and opacities in the vitreous were noted in the left eye. At that time the injured eye showed a moderate degree of mixed injection, brownish discoloration of the sclera near the limbus, suggesting rupture of the globe, and hemophthalmos. This eye was enucleated and the patient given mercury by inunctions, iodides by mouth and a cinchophen derivative intravenously. Within three months the uveitis of the uninjured eye cleared up, and it did not recur during the subsequent eighteen months

(final vision, 20/20). Pathologic examination of the injured eye revealed a large rupture of the sclera and the typical picture of sympathetic ophthalmia. The iris and the lens were absent and must have been expelled from the eye at the time of the rupture. The favorable outcome of the uveitis in the uninjured eye was the reason for the publication of the case.

P. C. KRONFELD.

Toxic Amblyopia

TOXIC AMAUROSIS DUE TO QUININE: TREATMENT WITH SODIUM NITRITE ADMINISTERED INTRAVENOUSLY. L. PELNER and E. SASKIN, J. A. M. A. **119:** 1175 (Aug. 8) 1942.

The patient was a Negro woman aged 69 years. There was a history of repeated attacks of malaria. On the third day of medication, after 40 grains (2.6 Gm.) the patient first complained of dimness of vision, ringing of the ears and moderate deafness. One more dose of quinine was administered by a member of the family. On examination the patient was found to be totally blind. The fundus of each eye showed extreme pallor of the retina with strong contraction of the blood vessels. Prostigmine methylsulfate solution hypodermically and sodium nitrite were given without apparent effect. On the fourth day after the quinine therapy was begun the pupils were dilated and did not react to direct or consensual light stimulus. There was a large area of edema extending from each optic papilla temporally passing above and below the macula and beyond it for a distance 1 disk diameter. A cherry red spot was present at each macula. The arteries were decidedly contracted and the veins somewhat dilated. Both papillae showed pallor and blurring of the margins. The intravenous administration of sodium nitrite solution produced a rapid improvement in vision. Two weeks later the corrected vision was 20/30 + in each eye. There was an almost concentric 10 to 15 degree contraction of the field for white. Slight pallor of the papillae remained. The vein-artery caliber ratio was still 2:1.

W. ZENTMAYER.

Society Transactions

EDITED BY DR. W. L. BENEDICT

NEW YORK ACADEMY OF MEDICINE, SECTION OF OPHTHALMOLOGY

KAUFMAN SCHLIVEK, M.D., *Chairman*

BRITTAIN PAYNE, M.D., *Secretary*

May 18, 1942

Congenital Anterior Synechias, Corneal Opacities and Microphthalmos. DR. FREDERICK H. THEODORE.

Two cases of congenital corneal opacities associated with anterior synechias and microphthalmos occurring in sisters were presented. In the younger sister, 6 years old, only the right eye was involved. A dense opacity occupied the posterior half of the cornea, with broad bands of iris tissue adherent to it. The adhesions arose mainly in the angle of the anterior chamber. In the older sister, 11 years old, both eyes were affected. The left eye was similar to that of her sister, but the right eye showed only a large zone of peripheral opacification merging into the angle tissue.

Lesions such as these were originally considered due to inflammation occurring either in fetal life or shortly after birth. Later, on the basis of extensive microscopic studies, most authors decided that they are due to a developmental defect occurring early in embryonic life. Peters stated the belief that they are the result of delayed or faulty separation of the lens from the surface ectoderm. Collins and Seefelder both said that they come about because of a faulty development of the mesoderm that grows in to form most of the cornea, including the endothelium, the anterior chamber and the anterior portion of the iris.

The cases presented are important in that the occurrence in sisters may confirm the developmental theory and, since most of the synechias arose from the angle of the iris and in one eye, the abnormalities were all peripheral and should tend to substantiate both Collins' and Seefelder's views. It is probable that all three theories are correct and operate in different cases.

DISCUSSION

DR. A. L. KORNZWEIG: I just want to say a few words about the possible embryologic basis for this interesting condition. Such anterior synechias must occur early, especially those that are centrally placed. When the lens separates from the surface ectoderm, the mesodermal tissue moves in to fill the space between lens and surface epithelium. The anterior chamber forms and divides the mesoderm into a nonvascular anterior portion, which forms the cornea, and a vascular posterior portion, which forms the pupillary membrane and the stroma of the iris. The

beginning of the anterior chamber is at about the sixth week of embryonic life. It is at that time that the central synechias will form. Later on, the anterior chamber deepens peripherally, and it is then that the peripheral synechias will appear. The synechias may be due to a local inflammatory process at this stage, but more probably are due to a general retardation of growth of the eye, as shown by the smallness of the eye and the retention of some atavistic features. The third possibility is a failure of Descemet's endothelium to form completely. In those areas where there are defects, anterior synechias may occur.

Tumor of the Optic Nerve. DR. WILLIAM B. AGAN (by invitation).

The case was reported of a white woman aged 37 with no family or previous history relevant to the ocular condition. In January 1938 she was employed by a jeweler. She was polishing a ring when it slipped from a vice and struck the right eye. There was no trouble until about six months later, when she noticed an occasional dull ache in the eye. She felt that her vision in this eye was not as good as it had been. In December 1938 she consulted an oculist, who found the vision to be 20/30 — 2 in the right eye and 20/15 in the left. With a + 1.25 D. cyl., axis 90, he was able to correct the right eye to 20/15. At that time he noted "marked sheathing about the vessels as they come off the disk." He found no pigmentation. There was no note as to the appearance of the left disk.

On Dec. 30, 1941, the patient came to me because she was bothered by an occasional blurring of the vision of the right eye. Refraction gave the following results: left eye, 20/65 without correction and 20/20 with a correction of — 0.25 D. sph. ⊃ + 1.25 D. cyl., axis 90; left eye, 20/20 without correction and 20/20 with a correction of + 0.50 D. sph. ⊃ + 0.50 D. cyl., axis 90. The perimetric field was normal, but the blindspot was slightly enlarged. Fundus examination revealed a pigmented mass on the right disk. This mass almost covered the disk, leaving a free area above and temporally. It extended out over the retina. The color was dark gray. The margins were sharply defined. There was about 3 D. of elevation. There were some newly formed blood vessels on the surface. The left eye showed no pathologic change.

At least twenty-five ophthalmologists examined the eye, and all agreed that the tumor was probably a malignant melanoma. One oculist made the diagnosis of a "congenital pigmented cyst."

On Feb. 19, 1942 the eye was enucleated at the Brooklyn Eye and Ear Hospital. Dr. Edgar Burchell, of the New York Eye and Ear Infirmary, prepared the specimen and made the slides. Kodachrome pictures and sections were sent to Dr. Theodore Terry and Dr. Frederick Verhoeff, in Boston.

Dr. Verhoeff's opinion was as follows: "The tumor is identical with the nonmalignant melanoma arising from the lamina cribrosa. The optic disk often contains chromatophores. Judging from the kodachrome view, I think I would have advised enucleation on the assumption that the growth was a malignant melanoma. The sections sent to me showed the tumor confined to the optic disk, but the kodachrome view seems to indicate that it also involved the choroid. I suppose sufficient sections were made to determine whether it did so. If it involved the choroid, it would be less remarkable than if it was confined to the disk."

Dr. Terry wrote: "I have studied the sections with interest and have Dr. Mallory's opinion. We agree that this specimen represents the most benign form of so-called malignant melanoma. According to Callender, it should be a 'spindle A' type. In my opinion, it would take several years to fill the globe, but its extension to the chiasm might occur in less than a year. I consider its malignancy as approximately that of a basal cell carcinoma. I believe it originated from the pigment-bearing cells in the lamina cribrosa, and its growth into the eye is a natural consequence of its location. It is my feeling that this theory is more logical than the assumption that it arose from remains of Bergmeister's papilla. Pigment cells do occur in the lamina, but, so far as I know, melanotic pigment has no reason to develop in the papilla unless there is considerable maldevelopment in this region associated with a coloboma."

The following opinion is that of Dr. Bernard Samuels: "A small cyst is present in the ciliary body. Posteriorly, except in the choriocapillaris, the choroid shows unusual pigmentation, especially near the emissaria of the posterior ciliary vessels. The nerve fiber layer is edematous, with a neuritic roll on each side. The scleral and choroidal canals are filled with a coal black mass. Because of the narrow opening through the lamina vitrea, this mass mushrooms into the eye. The foot rests on the lamina cribrosa, the neck is restricted and the head replaces the papilla. The mass follows a columnar arrangement in the nerve fiber bundles. The nerve fiber layer is invaded anteriorly, and there is a tendency to proliferation of cells along the walls of the blood vessels. On one side, the neuritic roll is invaded by some of the pigment epithelium. The pigment epithelium shows fragmentation at some points and hypertrophy at others. Several small drusen are noted. A few cells have invaded the retina. Within the choroidal canal, in some sections tumor cells continue into the stroma of the choroid and the sclera. Recession of the lamina cribrosa and bulging of its sides produce an ampulla-like formation filled by the tumor. Posterior to the lamina cribrosa is a smaller pigmented mass, connected with the larger mass, and its posterior extremity is not sharply defined. Bleached sections show the tumor cells to be well differentiated and spindle shaped. The pigment is intracellular, and no miotic figures are seen. From a histologic point of view it resembles a highly pigmented melanoma of the choroid. The sclera about the disk contains large numbers of chromatophores, from which the tumor seems to arise, but it is not possible to say whether the tumor springs primarily from the chromatophores of the sclera, from the choroid or from the lamina cribrosa. Diagnosis: melanoma of the papilla, optic nerve, choroid and sclera."

DISCUSSION

DR. BRITTAIN F. PAYNE: Dr. Samuels examined this section. (A slide was shown.) As can be seen, the extent of the growth is upward through the lamina cribrosa. Dr. Samuels was of the opinion that the tumor might have arisen from the choroid and extended into the lamina cribrosa. The fact is that the tumor is definitely in the disk, and the chances are that it did arise from the lamina cribrosa. The depigmented slides show cells which greatly resemble those of epithelial origin. It is

possible that the tumor arose from embryologic rests of the primitive optic cup or from the pigment epithelium. Cross sections of the nerve a little farther back show peculiar openings between the nerve bundles and also in the nerve bundles themselves.

DR. RALPH I. LLOYD: Since observing this case, I have gone through the literature looking for a similar one, and I found a case reported by Ogawa in which the microscopic picture was much like the slides Dr. Burchell has shown of the tumor in Dr. Agan's case. There is no history, because the eye was from a Japanese officer, removed because of a penetrating wound. As an officer of his rank required perfect visual acuity; it is assumed there was nothing of which he might complain. Dr. Reese has submitted a slide showing a picture almost exactly like that in Dr. Agan's case. The patient was under observation for eighteen months without change in visual acuity or in appearance.

The surface of Dr. Agan's tumor of the disk was smooth, the vessels were sheathed in embryonic remains, as in Dr. Levitt's case, and there was no indication of breaking through from the rear. The mass was solid, and the binocular ophthalmoscope did not penetrate as in Dr. Levitt's case. It is impossible by ophthalmoscopic examination to determine the character of microscopic cells in a mass like this. It is some satisfaction to know that the clinician was not the only person in doubt; four pathologists did not agree entirely.

Congenital Absence of Lacrimal Puncta in Three Members of a Family. DR. ARNO E. TOWN (by invitation).

This article will be published in full, with discussion, in a later issue of the ARCHIVES.

Reconstruction of the Lower Eyelid. DR. BERNARD FREAD.

A 52 year old man with a ten year history of a recurrent basal cell carcinoma was treated with radium and roentgen ray therapy and endothermy. A cicatricial ectropion of the right lower eyelid formed with imperfect lid closure.

The first operation consisted of formation of lid adhesions with excision of bands of scar tissue and filling in of the defect in the skin with a free skin graft from the left upper eyelid. Three months later the adhesions were severed. The basal cell carcinoma recurred in spite of further endothermy and heavy doses of roentgen rays. The lid margin and the conjunctiva became involved, and two years later a second operation, according to the technic of Dr. Wendell Hughes, was performed as follows:

The inner three quarters of the right lower eyelid was excised, and the defect was filled in with a tarsoconjunctival flap from the right upper eyelid, the upper lid being split into two layers. The defect in the skin was filled in with a graft from the right upper eyelid. About seven months later new "cilia" were formed by the placing of a graft from the right eyebrow for the upper lid "cilia" and from the left eyebrow for the lower lid "cilia." The cosmetic and functional results were good when the new eyelids were divided.

DISCUSSION

DR. RUDOLF AEBLI: The problem of plastic repair in such cases is to reconstruct the lower eyelid if the entire thickness of the lid is lost. If the defect is only 10 mm. or so, one can repair it by splitting the remaining lid, undermining the edges and bringing the lids into apposition to close it. If the loss of substance is extensive, so that the entire inner three quarters of the lid has to be sacrificed, as in this case, then I think the method Dr. Hughes published in the ARCHIVES (Hughes, W. H.: New Method for Rebuilding Lower Lid, ARCH. OPHTH. 1008-1017 [June] 1937) is excellent, and that is the one which Dr. Fread followed in this case, with a good result.

Thrombosis of the Central Vein Treated with Heparin. DR. CHARLES M. ROSENTHAL (by invitation).

A case was presented in which a thrombosis of the central retinal vein existed five weeks before treatment with heparin was started.

On examination, the patient exhibited a typical "textbook" picture of a complete trunk occlusion of the central retinal vein. She was admitted to the hospital. Physical examination gave negative results except to show a diseased right tonsil. She was given a total of 180 cc. of heparin over a ten day period. The first dose was 20 cc. in 1,000 cc. of dextrose and saline solution. The next two doses were 10 cc. in 500 cc. of saline solution. The patient was then given the heparin undiluted directly into the vein.

The patient showed some improvement on the fourth day, and by the twelfth day the improvement of the retina was pronounced. In one month's time the fundus was practically normal in appearance, and two months after the onset of the thrombosis the vision, which at the time of the occlusion was 2/60, had returned to 6/7 — 2 with correction.

This case was interesting from the standpoint of the length of time the thrombosis had lasted before treatment was begun and the excellent visual result obtained.

DISCUSSION

DR. JOSEPH LAVAL: I should like to report the history of a patient who had thrombosis of the central retinal vein in each eye. There was closure of the central retinal vein of the left eye in August 1938, with severe edema of the macular area, but the vision was 20/25. The patient did not receive any heparin; the vision remained 20/25 for three months, but the edema persisted, so that finally the vision was reduced to 20/40 and then to 20/50. Finally, a hole in the macula developed, and the vision was 10/400 two and a half years later.

In January 1942 the same patient, who had a blood pressure of 220 systolic and 140 diastolic, came in complaining of blurred vision of the right eye of three days' duration. The vision was 20/25 +, with closure of the central retinal vein, many hemorrhages and pronounced edema of the macula. The patient was hospitalized, and heparin therapy was instituted immediately. Before the use of heparin, the prothrombin index was 100 per cent, and the coagulation time was ten minutes. Twenty-four hours after the use of heparin was started, the coagulation time was thirty-three minutes, and the prothrombin index was 75 per

cent. Heparin was given intravenously at the rate of 20 to 25 drops per minute for three days. When its use was started, the patient received "dicoumarin" (3-3'-methylene bis [4-hydroxycoumarin]), which is not yet on the market. This was given by mouth in doses varying from 200 to 300 mg., the amount depending on the coagulation time, which remained between twenty-four and seventeen and one-half minutes. The prothrombin index was at one time as low as 25 per cent. The purpose of this treatment was not to dissolve the already existing thrombus, but to prevent propagation of the clot, which often occurs if no treatment is instituted.

Three weeks later the patient had 20/30 vision, and when I last saw her, on April 30, it had not changed. There was still some edema about the macula.

Whether heparin was of any benefit in this case I cannot say, because I observed the eye for only four months.

I saw a patient today, two weeks after closure of the inferior temporal vein, who came to me originally with 20/400 vision. At the end of two weeks without heparin, the vision is 20/40 +. I think many more patients will have to be treated with heparin before one can say that it is of benefit in the treatment of thrombosis of the central retinal vein or of its branches.

DR. KAUFMAN SCHLIVEK: I think much more work is necessary before heparin can be evaluated. There have been 4 cases of its use at the Mount Sinai Hospital, and I can only report that it failed in all. The treatment in the first case came about in a peculiar way. Dr. Lilienthal, who discussed heparin at one of the meetings of this society early in the season, long ago said, "Why don't you try heparin?" Soon after that I had a patient with thrombosis of the central vein. Dr. Friedberg gave heparin intravenously by the continuous drip method with no result. I had another case in the hospital, and then two others, in all of which the treatment was a complete failure. Before conclusions can be drawn, a great many more cases will have to be observed. Many ophthalmologists have seen patients with thrombosis of the central vein who retained fairly useful vision, 20/50 or 20/40, without heparin.

Modification of Wheeler's Tarsorrhaphy. DR. DANIEL B. KIRBY.

A case illustrating the results of a modification of Wheeler's tarsorrhaphy for use in widening and elongating the palpebral fissure associated with exophthalmic goiter was presented.

Spasm of the smooth muscle and certain degrees of edema of the orbital tissues may subside after medical treatment or after thyroidectomy, but in some instances the widening of the palpebral fissures and the proptosis may persist or even increase. In rarer instances they may progress to an extreme degree and be associated with cellular infiltration and vascular engorgement and may require radical drainage of the orbital tissues. In the milder conditions, there may be a disfiguring state of exposure of the eyes, which, even though it does not endanger the integrity of the cornea, renders the patient unhappy because of the discomfort and the knowledge that he is unemployable on account of his

appearance. In some instances, erosions and ulcerations of the cornea result from the lack of moisture and drying of the widely exposed surface.

If the principal cause of the exposure is the spasm or overactivity of the smooth muscle of the orbit, then the indication is for recession of the smooth muscle and of the levator of the upper lid. This may be done through the conjunctiva or through the skin. The retraction of the lower lid is not as easily overcome. The whole phenomenon may be corrected by section which produces paralysis of the cervical sympathetic chain, but this causes the undesirable features of Horner's syndrome. Tarsorrhaphy will not correct overactivity of the smooth muscle.

When the principal cause of the disfigurement is proptosis, the indication is for shortening and narrowing of the palpebral fissure by external tarsorrhaphy. There may or may not be overaction of the smooth muscle and of the levator, which requires its own correction. Viewed from the side, the globe is observed to be pushed forward, and there is usually exposed to view the purplish congested veins of the deep orbital tissues.

Wheeler measured the fissures carefully, vertically and horizontally, and then calculated the extent to which he planned to shorten the fissure. He removed the transitional epithelium from skin to conjunctiva on the lid margin and then the conjunctiva and skin, including the lashes and their roots, from the lower lid area, leaving a tongue of tissue, chiefly of tarsus, to be inserted into a sheath formed in the upper lid by splitting it along the gray line. This modification consists in leaving the skin, lashes and conjunctiva on the upper lid area instead of removing them. To do so simplifies and improves the procedure (1) by eliminating the difficulty of taking away all of the lash bulbs, which form distorted hairs if remnants are left, (2) by eliminating removal of conjunctiva which is closely adherent to the upper tarsus and (3) by eliminating removal of skin, thus making the plastic repair of the dissected area easier. Retention of the line of lashes is desirable because it gives a more normal and satisfactory appearance to the patient. A forward placement of the external canthus, particularly if the canthus is rounded at all, is disagreeable to the patient. A number of patients have been pleased and satisfied with the results of this modification of Wheeler's tarsorrhaphy.

DISCUSSION

DR. JOHN DUNNINGTON: I have had no experience with Dr. Kirby's modification of the Wheeler tarsorrhaphy and can only say that the operation as done by Dr. Wheeler gives a sharp angle and not a rounded one. In my opinion, it is superior to the so-called Fuchs tarsorrhaphy. One has to be careful about doing the latter as a cosmetic procedure, because the patient is not always happy over the result even though the surgeon considers it ideal, particularly when the operation is done on only one side.

Congenital Prepapillary Cyst. DR. JESSE M. LEVITT (by invitation).

A 15 year old girl had a grayish white cystlike elevation covering a part of the optic disk and extending beyond it at its lower, inner margin. It was two and one half to three times the size of the disk and surrounded by normal tissue. The retinal vessels at the lower part

passed in front of it; those at the upper part were veiled and sheathed in the tissue covering. Examination with the binocular ophthalmoscope demonstrated clearly the cystic nature of the elevation and in addition disclosed the presence of a loop within. The loop moved up and down behind the retinal vessels with every motion of the eye. The attachment and the origin of the loop could not be seen.

The cyst represented the persistence of Bergmeister's papilla. The movable loop resembled a large prepapillary vascular loop such as is not uncommonly seen coursing into the vitreous and then returning to the optic nerve head.

DISCUSSION

DR. PERCY FRIDENBERG: The interesting thing in this case is that vessels run from the disk forward into the hyaloid strand and then are distributed normally, so that it looks as if prepapillary cysts in some cases are dilatations of Cloquet's canal or of the hyaloid artery. In the first picture shown, the vessels in the persistent hyaloid strand were dimly seen until they penetrated the membrane.

DR. RALPH I. LLOYD: The character of the mass anterior to the disk was evident only when the binocular ophthalmoscope was used. The hand ophthalmoscope is a most efficient instrument; so the discovery of a moving loop within the mass, thought to be remains of some of the vessels of Bergmeister's papilla, was a tremendous surprise.

With red-free light, the sheathing of the retinal vessels in embryonic tissue and the course of the nerve fibrils across the cyst were evident. The study of this case with the binocular ophthalmoscope was helpful when Dr. Agan's case of prepapillary melanoma appeared.

Bilateral Pigmentation of the Retina with Macular Changes. DR. GERALD T. SCHWARZ (by invitation).

Congenital grouped pigmentation of the retina usually appears in sector-shaped areas and is rarely bilateral. Involvement of the macula by small pigment flecks in this type of pigmentation was reported by Welter in 1927 and by Lowenstein in 1941. No instances of macular degeneration were found in the reviewed cases of congenital grouped retinal pigmentation.

A 6 year old white boy came to the service of Dr. John H. Dunnington in the ophthalmic department of the Vanderbilt Clinic, Presbyterian Hospital, for treatment of esotropia. During the examinations, it was found that the periphery of each retina showed pigmentation of the congenital grouped type which did not follow the sector distribution. The macular regions showed pigmentary disturbance of a salt and pepper aspect with interspersed pinpoint yellow areas and one larger flat yellowish depigmented area below and temporal to the right macula. The visual acuity with hyperopic correction was 20/50 in the right and 20/70 in the left eye. Night blindness was not present.

Neurologic and psychometric examinations disclosed the speech to be retarded and the mental age that of a 3 year old child. The opinion expressed after these examinations was that the patient suffered from maculocerebral degeneration of the Batten-Mayou type.

This patient presented the unusual combination of congenital grouped pigmentation of the retina with maculocerebral degeneration.

DISCUSSION

DR. MILTON BERLINER: I think that the case reported may prove to be a connecting link between two conditions which are considered to be unrelated, grouped pigmentation of the retina and cerebromacular degeneration. I had the pleasure of seeing the patient a few days ago, and I was impressed by the fact that the macular changes seemed to resemble those of Batten-Mayou disease, which in many quarters is considered to be related to the juvenile type of amaurotic familial idiocy, or Tay-Sachs disease. Recently a case was reported by Dide and Van Bogaert in which the grouped pigmentation somewhat resembled that in Dr. Schwarz's case, suggesting a transition form lying somewhere between grouped retinal pigmentation and retinitis pigmentosa. The changes in Batten-Mayou disease are related to a lipoid dystrophy. This disease differs from amaurotic familial idiocy, or Tay-Sachs disease, in that in the latter the ganglion cells are more involved and the lipoid found is a lecithin, whereas in Batten-Mayou disease the infiltrate resembles a neutral fat. However, I think an interesting question in the case reported is whether a lipoid dystrophy is present, and I would suggest that Dr. Schwarz make some blood studies to see if there is any increase in cholesterol or, better, make a splenic puncture, if possible, to determine whether any lipoid-laden histiocytes are present.

DR. GERALD T. SCHWARZ: The cholesterol content was found within normal limits: 237 mg. per hundred cubic centimeters.

DR. MILTON BERLINER: Thank you. I made the suggestion because in the case described by Dide and Van Bogaert, histologic and histochemical studies disclosed an increased storage of lipoids. In their case the foveas were uninvolved but the condition was associated with extrapyramidal paralysis.

DR. A. L. KORNZWEIG: Is there any record of the fields or of night blindness in the case reported?

DR. CHARLES ALLEN PERERA: One of the interesting things about this type of lesion is the pathologic process involved. The lesion in congenital grouped pigmentation of the retina is in the pigment epithelium, and in most of the cases reported to date, including one I published in the ARCHIVES in 1939 (Perera, C. A.: Congenital Grouped Pigmentation of the Retina, ARCH. OPHTH. **21**: 108-110 [Jan.] 1939), no scotomas were found corresponding to the areas involved. I do not think the lesion in Dr. Schwarz's case is exactly like the ordinary type of congenital grouped pigmentation, but it may be related to the group of macular degenerations and retinal abiotrophies.

DR. BERNARD FREAD: I had a similar case in a young man who had fairly good central vision, 20/30 in each eye, but typical night blindness. The lesion did not progress at all. At one time the patient received massive doses of vitamin A with no result.

DR. GERALD T. SCHWARZ: No night blindness was observed in this child.

Epithelioma of the Cornea. DR. GEORGE N. WISE (by invitation).

A 62 year old man who had suffered periodic attacks of undiagnosed inflammation in both eyes since the age of 17 entered Vanderbilt Clinic in April 1942. Examination revealed an irregular opaque

growth on the right cornea with three fleshy, movable, vascular masses at the limbus. The regional lymph glands were not palpable. The left eye showed a vascularized corneal scar. Vision in the right eye was light perception and in the left eye was 7/200.

After a diagnosis of Bowen's disease was made, the patient was admitted to the hospital, and the tumor was totally excised from the cornea and the limbus. Three weeks after the operation, the eye was still injected, the cornea was completely epithelized, though cloudy and uneven, and a few vessels had extended into the cornea from the limbus. Vision was perception of hand movements.

Microscopic examination disclosed that the corneal epithelium was made up of tumor cells with a disorderly arrangement and shape. There were moderate numbers of mitotic figures and several Bowen "clumped" cells. Beneath the tumor was vascularized, chronically inflamed tissue. The basement membrane was not invaded, and the tumor had apparently been completely removed. At the periphery, the tumor tissue passed abruptly into normal epithelium. The pathologic diagnosis was Bowen's disease, or intraepithelial epithelioma of the cornea.

DISCUSSION

DR. WILBERT SACHS: The first thing I should like to say is that I am not acquainted with Bowen's disease of the eye. However, I have seen many patients with Bowen's disease of the skin, on the extremities, the body, the face, the scalp, the genitalia and the mucous membranes of the mouth, the rectum and the vagina. With lesions of the skin, it is often difficult to make a positive diagnosis on the basis of clinical findings alone. Usually a tentative diagnosis is made and is or is not corroborated by the microscopic picture. It is well established that Bowen's disease is a distinct entity and that it has a definite pathologic picture. Bowen's tumor is only one of the many varieties of epitheliomas. Dr. Wise has well described the pathologic picture. The disease belongs to the malignant retarded type of dyskeratosis. Although it may last as long as fourteen years, it is considered a malignant process. Until the growth breaks through the basal cell layer, it is not a Bowen tumor; when it does, then it belongs to the anaplastic type of neoplasm, and that is highly malignant. There are many types of intraepithelial epitheliomas, and Bowen's tumor is only one of them.

It should be remembered that Bowen's tumor can infiltrate and even metastasize as an anaplastic epithelioma. In many cases one does not find the margin; the embryonic type of basal cells may start directly from the basal cell layer. Dr. Wise spoke of the formation of keratinized cells on the surface. This process is not the usual one found in Bowen's disease; instead there may be oozing, parakeratosis or formation of crusts. The inflammatory process may be either of the basal or of the plasma cell variety.

Book Reviews

Atlas of Ophthalmic Pathology. Prepared by Major Elbert DeCoursey and Colonel J. E. Ash, Medical Corps, United States Army, under the auspices of the Academy of Ophthalmology and Otolaryngology, at the Army Medical Museum, Washington, D. C. Third edition, 1942. Price, $5. Pp. 136. Available on direct application to the secretary of the Academy of Ophthalmology and Otolaryngology at Omaha.

As the preface states, the third edition of the "Atlas of Ophthalmic Pathology" represents an attempt to reduce the price and thereby permit a greater circulation. This goal cannot be achieved without some sacrifice in quality. The photographic prints in the second edition are generally superior to the reproductions in the new edition in clarity of detail and in contrast and shading of tone. The text accompanying the plates has not been changed. The brief histories and the concise descriptions of the pathologic changes are in their uniformity of greatest value to students and instructors. Outstanding in this well selected collection are the chapters on vascular diseases of the retina and tumors of the eye.

The atlas will be useful to all who are somewhat familiar with ocular pathology. For the readers who are not experienced in this subject, it will be difficult to evaluate the black and white plates. Certainly emphasis should be placed on the advice of Ash to supplement the study of the atlas with slides.

LUDWIG VON SALLMANN.

Collected Reprints from the Wilmer Ophthalmological Institute of the Johns Hopkins University and Hospital, Volume VI, July 1938 to July 1942. Baltimore, Johns Hopkins University and Hospital, 1942.

This bound volume from the Wilmer Ophthalmological Institute, the sixth in the series, contains the collected reprints which have appeared between July 1938 and July 1942. They are sixty-eight in number and their subjects comprise many phases of laboratory and clinical investigations in the field of ophthalmology; they reflect great credit not only on the writers but on the inspiring leadership of the director of the institute.

ARNOLD KNAPP.